

THESIS

on

THE CONGENITAL FACIAL DIPLEGIA SYNDROME: ITS
CLINICAL FEATURES, PATHOLOGY AND AETIOLOGY.

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by

JOHN LOUIS HENDERSON.

M.B., Ch.B., M.R.C.P.E.

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A TYPICAL EXAMPLE OF THE CONGENITAL FACIAL DIPLEGIA SYNDROME.

INTRODUCTION.

Since von Graefe (1880) described a case of congenital facial diplegia more than sixty examples of the condition have been recorded. Brief accounts of only six cases are to be found in British journals, and nothing worthy of note has been written on the subject in this country; most of the major works, and many of the case records have appeared in German.

There has not been a comprehensive review since the beginning of the century. At that time the number of cases was too small to render an analysis of the clinical features of much value. Indeed, an analysis of a small number of cases is very apt to give a distorted impression of the truth in any condition.

About a year ago I met with the condition in an infant of five months old at the Royal Hospital for Sick Children in this city. The patient is typically affected. A perusal of the literature aroused my interest and it became increasingly clear to me that the condition has very distinctive features. I have now reviewed the literature most exhaustively and critically, and have collected sixty cases /

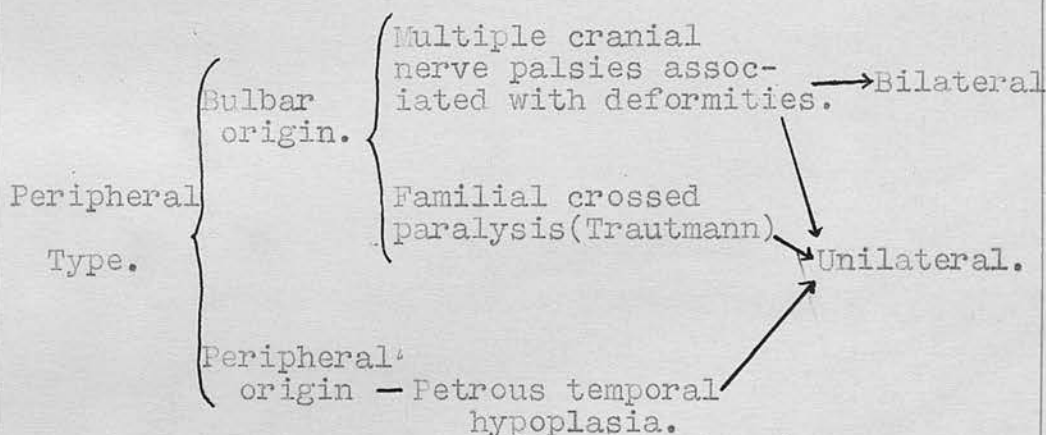
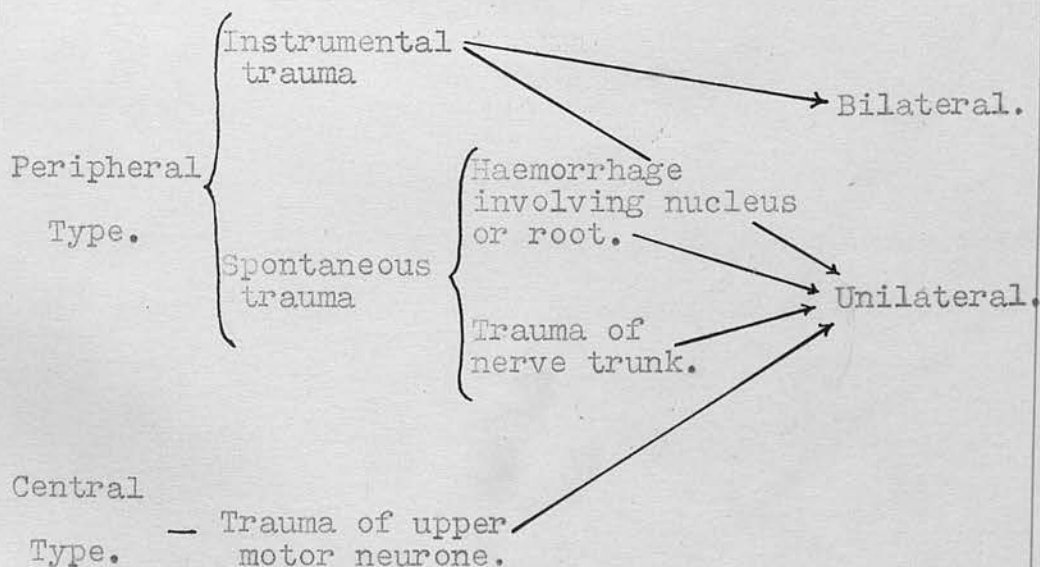
cases in addition to my own. It was found necessary to send to the Royal Society of Medicine and other libraries in London for a number of volumes, and a few photostatic copies of publications were obtained from the Surgeon General's Library in Washington. Forty of the cases were described in foreign languages, the majority being in German and French, while there were several in Spanish and others in Swedish, Dutch and Russian.

I think the term "Congenital Facial Diplegia Syndrome" a suitable one with which to identify these cases, it emphasises the most striking feature - the facial diplegia - and conveys the idea of an association of characteristic anomalies. The syndrome has been described under various names, the term "Infantiler Kernschwund" conveys a false impression and should no longer be used, while the terms "Infantile Oculo-Facial Palsy," "Agenesis of the Cranial Nerves," "Aplasia of Cranial Nerve Nuclei" etc., give no hint of the malformations of the limbs, etc., which are found so frequently.

Recent experimental embryology on mice with somewhat similar congenital anomalies suggests a possible explanation for the numerous abnormalities encountered in these cases. Hitherto their mode of production and correlation have remained obscure.

FACIAL PALSY IN THE NEWBORN.

Before approaching the principal theme in detail a résumé of the types of facial palsy encountered at birth will be helpful. I think the following classification an appropriate one:-

ANTEPARTUM.INTRAPARTUM.

The largest antepartum group is that which forms the subject of this paper. There is a smaller group with unilateral facial palsy but otherwise similar features. The third group with bulbar features was described by Dora Trautmann (1925) who observed six cases of congenital unilateral facial palsy in three generations of a family. There were contra-lateral pyramidal signs in three instances but none of them had any ocular or other defects, there was a psychopathic family history. Palsy of peripheral origin is characterised by deafness, auricular deformity - often gross - and sometimes by other local defects, all of the corresponding side; Marfan and Armand Delille (1901) demonstrated hypoplasia of the petrous temporal bone in their case with involvement of the facial nerve in the stenosed canal and secondary "atrophy" of the cells of the facial nucleus.

The intrapartum types only require passing reference. The bilateral variety is extremely rare, the blades of the forceps were held responsible for the diplegia in the cases of Seeligmüller (1892) and Edgeworth (1894); although the chances of bilateral forceps palsy are remote, the possibility is recognised, /

recognised, particularly in brow presentations. The common unilateral forceps palsy needs no comment, but that occurring in spontaneous delivery is rare; it occurs in cases of dystocia in which, in the position of asynclitism, the facial nerve is traumatised as it leaves the stylo-mastoid foramen. In the infant the nerve is exposed to external pressure in that situation as the mastoid process has not yet developed. The sacral promontory is usually the cause of the injury but the pubic body or rami are occasionally incriminated. The prognosis in all three peripheral traumatic types is good, incomplete recovery being unusual; it is less favourable in the uncommon supranuclear type resulting from trauma of the cerebral hemispheres and in those rare cases with intramedullary haemorrhage.

CASE REPORT.

E.O. Female. Aged 1 year, 10 months.

History:- The parents, a sister aged 12 and a brother aged 8, are healthy. Pregnancy was normal, and spontaneous delivery followed an uneventful labour lasting nine hours. The baby weighed about eight pounds. A peculiar facial appearance, bilateral convergent strabismus and club foot were all noticed shortly after birth by the doctor in attendance. The baby apparently nursed quite well although her mother maintains that she did not nurse as well as her other children; she was weaned when two months old. There was never any dysphagia nor nasal regurgitation.

The patient first came under observation at the age of five months, her mother complaining that she had never smiled nor moved her face, even when laughing and crying. She thought the infant had a film over her eyes for the first few weeks, and, as she did not seem to take notice until she was three months old, that she was blind. At that time the infant was well nourished and displayed an immobile expressionless face, severe bilateral convergent strabismus /

strabismus and a partially corrected talipes equinovarus on both sides. There was no ptosis and the eyelids could not be completely closed, there being an interval of about $\frac{1}{8}$ " during sleep.

As the child grew older the eyelids became more nearly approximated during sleep, and a slight but definite amelioration of the squint was observed. Recently, while eating, she has been observed to dislodge food from the cheeks with her hands. Orthopaedic measures begun soon after birth caused a great improvement in the position of the feet. Early doubts about the mental state were soon dispelled as the child grew older, the usual milestones appearing at the normal times. Dentition began at five months. Apart from a recent mild attack of bronchitis the general health has been good.

Examination.

A healthy looking, well developed female child. The forehead is tower-shaped and somewhat flattened towards the sides, the fontanelle is almost closed. The cheeks are plump and the periorbital regions rather hollow. There is bilateral epicanthus. The base of the nose is broad and the lower part has a squarish appearance owing to the flattened palsied alae /



alae nasi. The mouth is always slightly open and the upper lip prominent, during sleep it is opened more widely and assumes a triangular shape. The uvula is normal. The ears have a normal shape. There is no malformation of the pectoral or mammary regions. The only deformity shown by the limbs is the bilateral talipes equino-varus which is now almost completely reduced. The mental development and behaviour are quite up to standard.

NERVOUS SYSTEM.

Cranial Nerves.

The motor ocular nerves:- The head is moved in the direction of vision, horizontal and vertical. It is usually tilted to one or other side when fixing objects. There is a severe degree of convergent strabismus in both eyes. The only definite movement that can be elicited is the involuntary upward movement of the eye on the child attempting to close the lids. It would, therefore, appear that the superior rectus is still functioning in both eyes, certainly as far as this reflex is concerned. There is no ptosis indicating normal action of the levatores palpebrarum, the lids are now approximated during sleep. /



APPREHENSION.



CRYING.

leep. The pupils are normal in size, shape and reactions. The fundi show no abnormality whatever.

The facial nerves:- The face is immobile and expressionless at all times, indicating complete facial diplegia. There are no wrinkles in the skin of the face or forehead: winking is slow and feeble. Epiphora is also a feature. A little dribbling occurs from the corners of the mouth. Crying produces a whining noise with the usual interjections, and laughing a series of short pleasant phonations, - the former is accompanied by flushing of the face, but there is no facial movement in either. Speech, which is restricted to a few single words, is indistinct owing to inability to pronounce the labials, e.g. mā is ā. There was a complete lack of response of the facial muscles to both faradism and galvanism.

Other motor nerves:- There is no evidence of paresis in the muscles of mastication or in the soft palate, pharynx or larynx. There are no definite signs of lingual palsy and there is no deviation on protrusion (though the child cannot be induced to protrude the tongue beyond the lips), no asymmetry, wasting or fibrillary twitching.

Sensory /

Sensory nerves:- There is no gross impairment of any of the sensory functions.

There are no other demonstrable abnormalities of the nervous system.

Other Systems.

Normal. The thoracic and abdominal organs appear healthy.

Blood Wassermann:- Negative.

X.Rays:- Skull, spine and chest normal.

Summary.

Congenital facial diplegia, complete.

Congenital ophthalmoplegia externa, partial.

Congenital talipes equino-varus, bilateral.

Case No.	Year	Authors	Sex	Age	Facial Palsy	Abducens Palsy	Conv. Strab.	Ophth. Ext.	Ptosis	Trigeminal Palsy	Lingual Palsy	Mental Defect	Club Foot	Malform. Arm or Hand	Pectoralis Defect	Other Malformations &c.
					R. L.	R. L.		R. L.		R. L.	R. L.		R. L.	R. L.	R. L.	
1.	1880	v. Graefe	M	20	+	+										Epilepsy.
2.	1881	Harlan	M	18	+	+	+									Aplastic lachrymal caruncles.
3.	1882	Chisolm	F	35	+	+								+		
4.	1888	Moebius	M	50	+	+										
5.	1889	Schapringer	F	8	+	+					+					Hypoplastic lachrymal caruncles Bifid uvula. Epicanthus. "Other Abnormalities".
6.	1891	Bloch	M	7	+	+										
7.	1892	Fryer	M	16	+	+										
8.	1895	Kirmisson	M	7	+	+										
9.	1896	Procopovici	M	18	+	+										
10.	"	"	F	7	+	+										Epicanthus.
11.	1897	Schmidt	M	6	+	+					+					Ear Deformity. Deafness.
12.	1898	Thomas	M	21	+	+										Ear Deformity. Deafness.
13.	"	"	M	19	+	+										No tear secretion.
14.	1900	Heubner	M	17	+	+										Ear Deformity. No facial perspiration with pilocarpine.
15.	1901	Bernhardt	M	12	+	+										Ear Deformity. No facial perspiration with pilocarpine.
16.	1902	Koester	M	?	+	+										
17.	"	"	M	?	+	+										
18.	"	Decroly	M	7	+	+										
19.	"	Taylor	M	15	+	+										
20.	1903	Rainy & Fowler	F	52	+	+										
21.	1905	Batten	?	9	+	+										
22.	"	Gierlich	F	14	+	+										
23.	"	Guetzmann	M	12	+	+										Hypoplastic mammae. "Other Abnormalities".
24.	1908	Ziehen	M	18	+	+										
25.	1909	Collins	?	?	+	+										
26.	1910	Lennon	M	2	+	+										
27.	"	"	M	14	+	+										
28.	1912	Peritz	M	20	+	+										
29.	"	Welde	F	2	+	+										
30.	1913	v. Pfaundler	?	12	+	+										
31.	"	Beetz	F	22	+	+										Ear Deformity. Congenital dislocation of hip.
32.	"	"	M	20	+	+										Ear Deformity. Multiple bilateral defects of scapular muscles.
33.	"	"	F	7	+	+										Ear Deformity.
34.	1915	Snowball	F	11	+	+										
35.	1916	Kahlmeter	M	38	+	+										Infantilism.
36.	1917	Guetermann	M	7	+	+										Hypoplastic lachrymal caruncles
37.	1918	Fry	?	12	+	+										Epicanthus.
38.	1919	Fry & Kasak	F	11	+	+										
39.	1921	Abrahamson	F	4	+	+										Epilepsy.
40.	1922	Cadwalader	F	13	+	+										Deafness.
41.	"	"	F	10	+	+										
42.	1923	Kirby	M	52	+	+										
43.	1924	Cameron	M	3	+	+										
44.	1927	Van Gelder & Weyl	M	53	+	+										Ear Deformity.
45.	1928	Mandels	M	15	+	+										
46.	1929	Bonar & Owens	M	2	+	+										Epicanthus.
47.	1930	Alajouanine, Huc & Gopcevitch	F	6	+	+										
48.	"	"	F	5	+	+										
49.	"	"	M	12	+	+										
50.	"	"	F	4	+	+										
51.	"	Ullrich	F	8	+	+										
52.	1931	Yealland	F	16	+	+										
53.	"	Spatz & Ullrich	M	12	+	+										
54.	"	Allen	M	10	+	+										
55.	1932	Bielschowsky	F	9	+	+										Hypoplastic mammae. Pterygium Colli.
56.	"	Garrahan & Cucullu	M	2	+	+										Hyperthelia.
57.	"	"	F	2	+	+										Hydrocephalus. Epilepsy.
58.	"	Babonneix & Miget	F	5	+	+										
59.	1933	Gareiso & Barbieri	F	5	+	+										Bifid Uvula. Epicanthus.
60.	1935	Decourt & Ferrean	M	9	+	+										
61.	1938	Personal Case	F	12	+	+										Epicanthus.
					45	23	15	6	4	18	6	19	13	8		

The following cases were insufficiently authenticated to be included, but appeared to be genuine:- Procopovici (1896), Treacher Collins (1915), Cadwalader (1922), Ullrich (1930), Errecart (1930).
The following cases should not have been included as congenital conditions:- Recken (1891), Bach (1893).

TABLE I. Complete Table of Cases of Congenital Facial Diplegia in Chronological Order and Showing their Salient Features.

CLINICAL FEATURES.

A glance at the foregoing table will have shown the principal features of this congenital syndrome. Of fifty-seven cases in which the sex was stated there were thirty-four males and twenty-three females. It is the rule for the facial diplegia to be accompanied by palsies of other cranial nerves, particularly the ocular, the sixth pair being affected with remarkable constancy. The hypoglossal nerves are also frequently involved. All these congenital palsies are, of course, stationary from birth. The high incidence of congenital deformities is also an arresting feature; the chief of these is club foot which often occurs, while brachial deformity and pectoralis muscle hypoplasia have been observed on numerous occasions. Other malformations of a minor nature are frequently encountered. This outline of the principal features will now be followed by their individual consideration.

The Facial Diplegia. The facial palsy was usually observed during the first few days of life owing to difficulty with nursing and only partial closure of the eyelids during sleep. Quite often, however, /

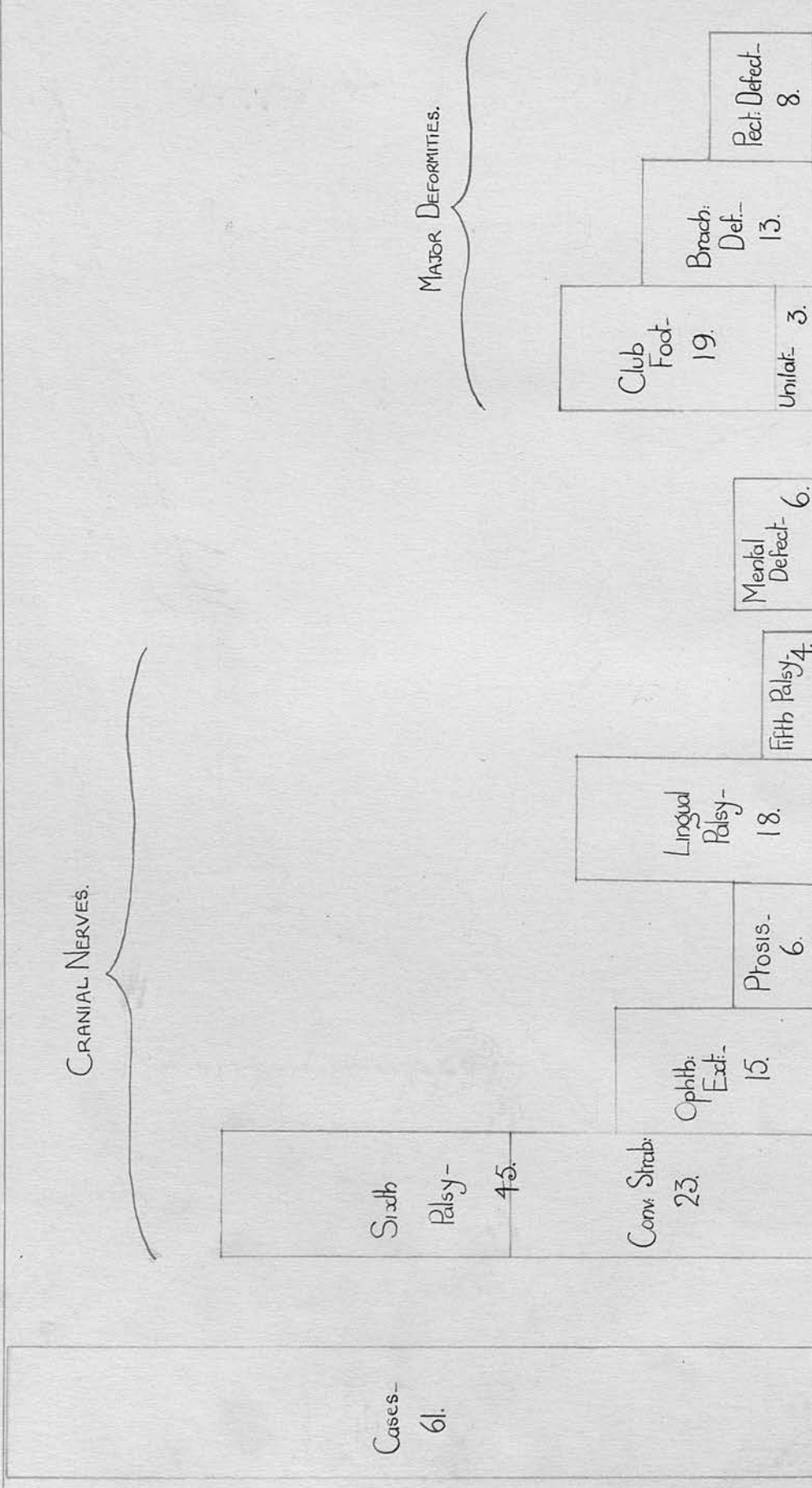


CHART I. INCIDENCE of the PRINCIPAL CLINICAL FEATURES.

however, it was not noticed for a few weeks or months when the inability to smile and the lack of facial movement on crying aroused the parents' concern. The most arresting feature of the facial palsy was, of course, the mask-like expressionless face which was most noticeable during laughing and crying. Corresponding to their immobility the face and forehead were devoid of wrinkles, but it was exceptional for the subcutaneous tissue or the skin of the face to be "atrophic."

It is an interesting fact that in some cases, as in my own, a slight diminution in the width of the palpebral fissures while asleep was noticed as infancy advanced. Lagophthalmos was, of course, another feature and the principal cause of the incomplete palpebral closure. The puncta lachrymalia were frequently slightly everted, thus accentuating the epiphora which was an almost constant feature. In older patients ectropion was apt to occur.

Inability to suckle in infancy has been alluded to already, quite often the difficulty was only slight, but in these cases it was often noticed that the nipple or teat was drawn further into the mouth than usual. Inability to close the mouth was the rule. Undue prominence of the upper lip was a striking feature; in adults the lower lip was usually everted and prominent also, dribbling of saliva from the corners of the mouth was a troublesome symptom.

Speech /

● = COMPLETE PALSY.

R.	L.	20 Cases.
●● ●●		
●● ●●		5 "
●● ●●		3 "
●● 		13 "
●● 		1 "
●● 		3 "
●● 		1 "
+		10 "

CHART II. Distribution of the Facial Paralysis.

Speech was nearly always indistinct owing to inability to close the lips and thus make labial sounds, e.g. ā for mā, ä for mǎp. While eating, food was apt to lodge in the cheeks, as in the present case, and it was returned to the mouth with the aid of the hands.

The degree and distribution of the palsy was analysed in fifty-six cases, five being discounted owing to insufficient data. It was incomplete in the majority of the cases, but of severe degree in nearly all of them.

Charts 2 and 3 indicate the frequency of total paralysis in the four facial quadrants. Twenty cases, almost exactly one third, exhibited a complete diplegia, while the predominance of complete upper facial palsy over lower was a striking feature of the incompletely paralysed group. When partial it was usually asymmetrical, though this was rarely more than slight; it was complete on one side in ten cases. In only ten cases was some movement possible in all four facial quadrants.

A more detailed analysis of the distribution is impracticable owing to the custom of describing the movements of the face in terms of regions rather than /

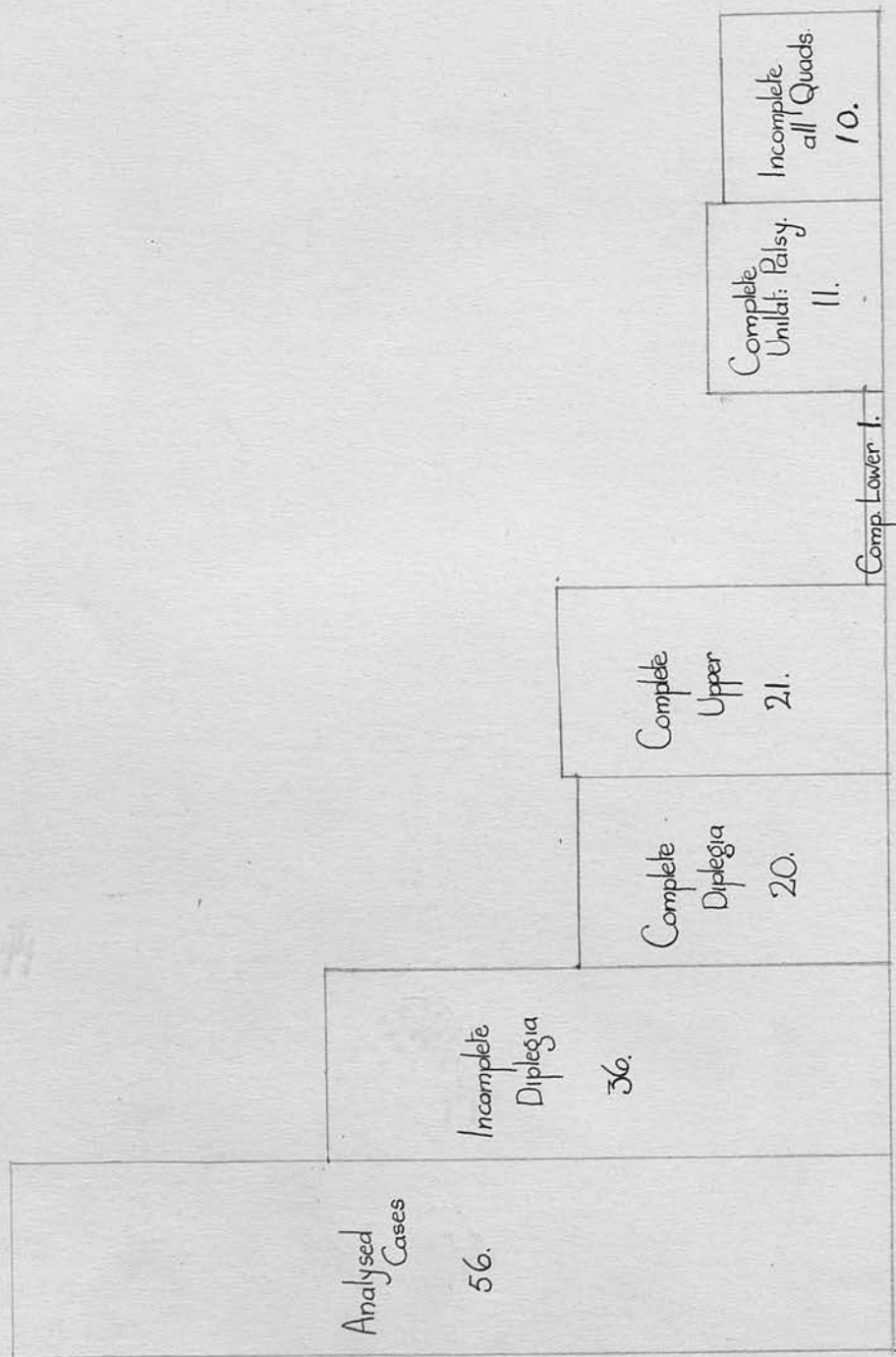


CHART III : DISTRIBUTION of the FACIAL PARALYSIS.

than muscles. It is clear, however, that those which draw the corners of the mouth outwards and downwards, including the platysmae, are much the most frequently spared. The frontalis muscles are those most constantly paralysed, the peri-orbital muscles are usually completely paralysed also, but occasionally contain a few functioning fibres. It is unusual for any of the facial muscles to escape completely and the degree of paresis is nearly always severe; this is a result of the sparseness of functioning muscle fibres in the paretic muscles.

The electrical reactions of the facial muscles were tested in twenty-three cases. There were no qualitative changes, but nearly always a marked quantitative reduction in the response of those muscles capable of some function. In a few instances muscles incapable of voluntary contraction showed a slight response, in the distribution analysis these have been regarded as paralysed muscles.

The characteristic distribution of the palsy contrasts sharply with the common supra-nuclear and infra-nuclear types and it may be of diagnostic value in the absence of the other features of the syndrome.

Only /

	Other Cranial Nerve Palsies.	No Other Cranial Nerve Palsies.
No. of Cases _____	51	10
Major Deformities _____	28	1
Minor Deformities only, excluding _____ Auricular	7	0
Auricular Deformity _____	4	4
Deafness _____	0	3
Mental Defect _____	6	0

TABLE II. The Contrasting Features of "Complicated" and "Pure" Facial Diplegia.

Only ten of the sixty-one cases were uncomplicated by other cranial nerve palsies and it may be significant that this group is almost free from the usual deformities. It is contrasted with the "complicated" group in table 2. The features of the facial palsy usually correspond with those of the "complicated" cases.

Ocular Manifestations. In those cases with convergent strabismus the ocular abnormality was usually noted at birth or shortly afterwards. In the absence of a squint ocular palsies sometimes escaped notice until later infancy. The parents were often concerned by the white appearance of the eyes seen between the incompletely closed lids during sleep, the reflex upward rotation of the eyeballs when the lids are closed only leaves the sclera visible in these cases. This appearance is sometimes attributed to "a film over the eyes" as it was in my case. A slight but definite amelioration of the convergent strabismus was observed in three of the cases of Alajouanine, Huc and Gopcevitch (1930) and I am quite satisfied that it occurred in the present case also. I believe this to be the result of an attempt at compensation by the functioning muscles with /

with the increasing co-ordination of ocular movements which occurs during infancy. It is difficult to see how this can occur in severe cases of ophthalmoplegia such as the present one, but the fact remains.

External ocular palsies, including ptosis, accompanied the facial diplegia in fifty cases, about five-sixths of the total.

Abducens paralysis, bilateral in all except two cases and rarely incomplete, occurred in no fewer than forty-five patients, thus contributing to the syndrome one of its most characteristic features. It is of interest to recall that Moebius (1892) thought it unlikely that facial diplegia could occur without an accompanying sixth.palsy. Abducens paralysis was the only ocular palsy in thirty-one cases; it was accompanied by oculomotor palsy in thirteen instances. Twenty-three, almost exactly half, of the abducens group had a convergent strabismus which was nearly always bilateral; that it does not occur more constantly is a feature of congenital sixth paralysis as opposed to the acquired form. The reason for the absence of strabismus in so many cases probably lies in the close functional association /

association of the medial and lateral recti and their intimate cerebral connections; this accounts for the paresis of the medial recti which can sometimes be demonstrated.

External ophthalmoplegia, always bilateral, occurred in fifteen cases; it was contributed to by abducens palsy in thirteen of these. The ophthalmoplegia was usually of severe degree but rarely complete, the only example of this was the infant of Spatz and Ullrich (1931). Internal ophthalmoplegia never occurred.

Ptosis, always bilateral, but usually only partial, occurred in six cases. In three cases it was the only cranial nerve palsy to accompany the facial diplegia, in another it complicated a slight unilateral abducens paresis, while in the remaining two cases it was associated with ophthalmoplegia externa.

There has been but little reference to trochlear involvement, probably owing to the difficulty of assessing it - especially in children; however, the available evidence indicates that it is liable to be affected along with the oculomotor nerve.

Amblyopia was not a feature of these cases, but refractive /

refractive errors and astigmatism frequently occurred.

Owing to the feebleness of winking and the incomplete closure of the eyelids during sleep the corneae and conjunctivae are poorly protected, and recurrent or chronic conjunctivitis frequently occurred. Corneal opacities were unusual but were not unknown in adult patients.

Lingual Features. Paresis and hypoplasia of the tongue occurred in eighteen cases, it was always associated with ocular palsy. It involved both sides in ten cases, but was rarely symmetrical; it was unusual for the palsy to be severe, though it was so in a few cases. The degree of wrinkling corresponded to that of the subjacent hypoplasia and characteristically, on protrusion, which was sometimes very limited, the tongue deviated towards the weaker side. Fibrillary twitchings of the tongue were noted in two instances, but too much significance cannot be attached to them in view of the static condition of the lingual and other palsies from birth. The dysarthria resulting from the facial palsy and the difficulty in moving food about the mouth were accentuated in proportion to the severity of the lingual /

lingual involvement.

Trigeminal Palsy. It was unusual for the muscles of mastication to be affected. Masticatory difficulty was encountered in four cases, it affected both sides in three of them, but was never severe. The striking feature was the inability to perform lateral chewing movements.

Paresis of the Soft Palate. In many of the cases no reference was made to the throat, presumably owing to normal findings in most of them. There were four instances of bilateral paresis of the soft palate, six of dysphagia, in three of which it ceased in infancy, and four of nasal regurgitation in infancy. Three of the cases with dysphagia and regurgitation had lingual palsy which might partly account for the difficulty. It is impossible to assess the exact cause of these symptoms. In no case was there evidence of gross vagal dysfunction: the nerves responsible for the paresis of the soft palate are distributed via the vagus but originate in the accessory nuclei.

The Club Foot. This malformation occurred in nineteen cases, almost one third of the total, it was bilateral in sixteen cases. The deformity was one /

one of talipes equino-varus in every case with the single exception of that of Kirmisson (1895) which had the usual deformity on the right and a calcaneo-valgus deformity on the left. In most of these cases the deformity had been partially or wholly corrected in infancy.

The fact that there were ten instances of club foot in the last fifteen cases published, whereas only nine so complicated had previously been recorded, calls for comment. It is probably due to the erroneous emphasis placed on the rarity of the anomaly in this syndrome by Alajouanine, Huc and Gopcevitch in 1930, this will be referred to again.

Other deformities of the foot, such as syndactyly, have never been recorded.

Pectoralis Muscle Defect. Hypoplasia of the pectoralis muscles was a feature in eight cases; it was always unilateral and associated with mammary hypoplasia of the same side. The condition was described in detail in only three cases, and these were quite typical; all showed a complete absence of the sterno-costal part of the pectoralis major, while the minor was absent in two of them and poorly developed in the other. The clavicular part of the major /

major muscle was only slightly affected or had escaped altogether. In the case of Mandels (1928) the third, fourth and fifth costal cartilages were defective and the hypoplasia involved other muscles of the chest and arm on the same side; the association of local skeletal anomalies with pectoralis defect is not infrequent. In three cases there was brachial hypoplasia of the same side. The defect occurred six times on the left side and twice on the right side. In the case of Schmidt (1897) there was a large skin fold passing from the third rib to the middle of the upper arm on the side of the defect.

Mention may be made here of the unique case of Beetz (1913) - Case No. 32 - a youth of twenty years whose pectoralis muscles did not appear defective, but who exhibited a hypoplasia of the serratus anterior, infraspinatus and latissimus dorsi muscles on both sides, and of the trapezius in all three parts, the levator scapulae and the supraspinatus muscles on the right side.. The serratus anterior was completely absent on the right and poorly developed on the left.

It /

It is of interest to recall that of muscle defects in general, those of the shoulder girdle are much the most frequent, while of the rarer situations, those of the abdominal wall hold first place. Abromeit (1909), in his large review of cases, found the following incidence:-

Pectoralis defect	-	187
Trapezius "	-	33
Serratus anterior "	-	21
Abdominal muscle "	-	11
Numerous others less frequently.		

Bilateral defect was very rare, which adds to the interest of the case of Beetz described above.

Malformations of the Arm and Hand. Brachial malformation was encountered in thirteen cases, it was confined to the hand in nine of these, and there was under-development of the arm in four others. Apart from the case of Mandels in which the only reference to the arm was "weak development of the muscles of the left arm" there was hypoplasia or dysplasia of the hand in all cases. There was one instance of congenital amputation of the hand, four in which the hand was "much smaller" than the other, and another had a club hand; two of these cases also had syndactyly. In the remaining six cases the malformation was confined to the fingers, in /

in two there was brachydactyly and syndactyly - in one of which it was bilateral, in three others there was syndactyly alone - bilateral in one instance -, and another exhibited deformity of an index finger. Syndactyly occurred in seven cases and was accompanied by hypoplasia of the hand or fingers in four. In only two instances was the malformation bilateral and this of the fingers alone. The two sides were affected with almost equal frequency. Three of the four cases with brachial malformation were associated with pectoralis defect of the same side, whereas none of the nine cases with hand involvement alone had this defect. Five cases were associated with club foot.

Minor Congenital Anomalies. In a few instances these have been disposed of as "other abnormalities" but in the great majority they have been enumerated. In several cases the root of the nose was broad and rather flat. Bilateral epicanthus occurred in six cases in two of which it was associated with hypoplastic lachrymal caruncles. Another case had aplasia of lachrymal caruncles. There were eight instances of ear deformity, they were all slight and usually bilateral, and the malformation was confined /

confined to the ear lobe in each one; two of the three deaf cases fall into this group. Arched palate was noted four times and bifid uvula twice. In addition to those cases exhibiting pectoralis defect, with which mammary hypoplasia is always associated, bilateral mammary hypoplasia occurred in two cases in which the pectoralis muscles appeared normal.

The pterygium colli depicted in the atypical case of Ullrich (1930) will be referred to in the discussion on aetiology.

Only a few cases exhibited functional anomalies which were probably congenital. Heubner's case (1900) had a total lack of tear secretion; this was also observed by Bernhardt in two cases of the analagous unilateral facial palsy. Köster (1902), in his two brothers, noted an inability to stimulate sweat formation on the face. The case of Kahlmeter (1916) presented several unusual features the nature of which is uncertain, the chief of them were infantilism, vaso-motor disturbances in the legs and a high sugar tolerance. Three cases were epileptic and a fourth had fits in the first two years of life, none of these were regarded as mentally defective.

Mental /

Mental Defect. In six cases there was clear evidence of subnormal mentality, four of these had reached adolescence or adult life, and the other two were young children. The amentia did not appear to be very severe in any of these patients. A few other cases in infancy or early childhood were described as backward or possibly mentally defective; a study of the available facts leaves one with the impression that, owing to the retarding influence of their multiple physical handicaps, a diagnosis of mental defect should usually be postponed in such cases.

The Analogous Unilateral Facial Palsy Group.

The variant of the syndrome with unilateral facial palsy is less frequently encountered. The palsy has the same distribution and characters as that seen in the bilateral cases. There is a greater tendency for the facial palsy to be uncomplicated in this group; and excluding abducens paralysis which occurs in about half of the cases, other cranial nerve palsies and structural defects of the limbs, etc., are infrequent. The abducens paralysis is usually bilateral, but occasionally only homolateral.

Among others, cases have been recorded by:-
Schultze (1892) /

Schultze (1892), Bernhardt (1894) (1897), Warrington (1897), Langdon (1899), Stéphan (1900), Minor (1900), Lagrange (1901), Comby (1901), Souques (1903), Babonneix and Miget (1932), Dupuy-Dutemps (1934) and Bálint (1936).

PATHOLOGY.

It is unfortunate that pathological evidence is available in only three of the published cases. They are those of Heubner, Rainy and Fowler (1903) and Spatz and Ullrich. It is important that the principal macroscopic and histological features of these cases should be described.

Heubner's case. - A boy, aged one year and seven months; died of broncho-pneumonia. The chief clinical features were congenital facial diplegia, bilateral abducens palsy and left lingual hemiparesis and atrophy. The facial palsy had remained unchanged from birth; it was complete on the left side and of typical distribution on the right side, the muscles at the corner of the mouth being incompletely paralysed. There was no spasticity of the limbs. The more delicate functions of nervous control could not be tested on account of the age and mental retardation.

The complete neuro-muscular units of the affected parts were not examined, only the brain and cord being retained. Macroscopically an asymmetrical medulla oblongata was evident, the left half was smaller /

smaller than the right, and some of the tissue underlying the pyramid had a shrunken appearance. The nerves issuing from the medulla did not look grey or atrophic, the second and third pairs and the left trochlear nerve looked normal, while neither the right trochlear nor the abducens nerves could be found.

Histologically the most notable abnormalities were seen in the series of motor nuclei, they were marked in the sixth, seventh and twelfth and slight in the third and eleventh. The sixth pair showed the most striking changes, both showing almost complete absence of ganglion cells. In the seventh and twelfth pairs the left sided nuclei were the more abnormal, the right contained a diminished number of cells but were provided with normal ganglion cells to a certain extent. Corresponding to the cells the roots of the nerves were lacking or sparsely developed. Further up towards the cerebrum this crippling of the motor nuclei ceased, only in the left third nucleus was there slight evidence of it. Distally a similar picture was present in the left accessory nucleus. The fourth nuclei were not specially mentioned, the fifth, the ninth, and the tenth were normal. The anomaly was not limited to the /

the nuclei however, The medial longitudinal bundle was very hypoplastic on both sides, this corresponding in degree and extent with the affection of the nuclei. The formatio reticularis was, on the whole, sparsely developed, particularly on the left; the interstitial tissue was more affected than the nerve cells, while those nerve cells present were well developed. Both olives were hypoplastic, particularly the left, the diminished number of nerve cells were normal in appearance. Further, on the left not only the fibres of the pyramidal tract streaming out from the motor nerve nuclei appeared to be lacking, but the whole pyramidal bundle even in the distal part of the medulla seemed to show scanty development. The whole structure of the cord looked rather retarded, but the cells were all normally developed. Marchi's stain failed to show any degenerative changes in the brain or cord.

Rainy and Fowler's case. - A girl, aged ten weeks; forceps delivery; died of broncho-pneumonia. The facial diplegia was almost complete, only slight contraction of a few medial fibres of the right frontalis and drawing down of the right mouth corner occurring; there were no other nerve lesions and no structural anomalies. The whole neuro-muscular unit /

unit of the seventh pair of nerves was examined. The brain and nerves appeared normal but there was gross "atrophy" of the facial muscles.

Sections from the second cervical segment to a point above the third nucleus were examined. The only abnormalities seen were in the seventh nerves and their nuclei. Both nerves showed marked degeneration, the ascending part of the root, the fasciculus teres and the emergent portion alike. "In the nuclei a large number of the cells ordinarily present had disappeared whilst those which remained presented a distinctly atrophic aspect, their processes being ill developed, the Nissl's bodies irregular and the cells themselves much smaller than one would have expected. The apparently healthy cells of the sixth nuclei afforded a marked contrast to those of the seventh." Like the roots, the nerve trunks showed advanced degeneration. The few fragments of muscle which could be found were normal histologically.

Spatz and Ullrich's case. - A boy, aged three months; died of broncho-pneumonia. The facial diplegia was complete apart from drawing down of the left mouth corner, and there was complete ophthalmoplegia externa. Syndactyly was the only other /

other anomaly.

Relative smallness of the pons and medulla oblongata was conspicuous, but the pyramid and olive were normally formed. The third and seventh pairs of nerves were very thin, the sixth was absent and the others appeared normal. No naked eye changes were seen in the hemispheres and brain stem on sectioning.

Histological changes were seen in the third, fourth, sixth and seventh nuclei. The sixth was the most severely affected, the nucleus and root fibres being completely absent. The seventh nuclei were unduly small but of normal appearance, and the roots were also small. The fourth nuclei were not in the usual place but were represented by scattered motoric elements lateral to it, the root fibre bundles were very small. The nerve cells in the third nuclei were reduced in number and the roots were consequently small.

Bálint (1936) reported the autopsy findings in an infant of three months old with congenital sixth and seventh palsy on the left side. The facial palsy was atypical, being incomplete in the frontalis and orbicularis oculi and the triangularis and mentalis, /

mentalis, while there were twitchings in the muscles. Micrognathia was the only structural defect.

Histological examination revealed a degenerative process. There was almost complete destruction of the left abducens nucleus and considerable damage to the right, with a lesion involving the fasciculus teres of the left facial nerve causing secondary degeneration of the nucleus. No detail is given in the report, only these bare facts.

Commentary. The striking similarity of the findings in the typical cases of Heubner and Spatz and Ullrich would appear to strengthen the evidence they afford in favour of typical cases of this syndrome being due to an **aplasia** or hypoplasia of the motor nuclei. Heubner's case, with extensive nuclear lesions, also demonstrates the occurrence of a widespread hypoplasia of nervous elements in some cases.

Rainy and Fowler's atypical case of uncomplicated facial diplegia with degenerative changes of the seventh nerves and nuclei may have been due to forceps trauma of the facial nerves, as suggested by Zappert(1910). It suggests that some of the cases without multiple cranial nerve involvement and /

and structural defects may also be of a similar nature. However, the fact that the facial palsy is usually of typical distribution would seem to align most of them with the more typical cases of the syndrome.

Bálint's case of unilateral sixth and seventh palsy, in the absence of illuminating evidence, may have been due to an intrapartum haemorrhage in the medulla. The last two cases demonstrate how much more doubtful is the nature of the process when the disturbance hinges on a local lesion, than when it is more extensive, and is supported by the collateral evidence of congenital deformities.

In the congenital eye muscle palsies absence and hypoplasia of the muscles concerned has frequently been observed at operation. Degenerative changes which involve the nuclei are sometimes the cause of the palsy, these are usually the result of small intrapartum haemorrhages in the brain stem. Nuclear agenesis has seldom been demonstrated but the fact that it occurs was recently demonstrated by Phillips, Dirion and Graves (1932); in a child of five years with congenital bilateral abducens palsy they found a hypoplasia of the sixth pair of nuclei and nerves.

HISTORICAL REVIEW.

The writings of Moebius on the subject of "Infantiler Kernschwund" in 1888 and 1892 attracted considerable attention and excited a good deal of controversy. He regarded congenital cranial nerve palsies and those acquired in infancy and early childhood as fundamentally the same. He classified the forty-three cases of cranial nerve palsy in young children which he collected into six groups; one of these was combined sixth and seventh palsy of which he described six cases, the first five of this series and the case of Recken (1891) which was acquired. Moebius thought that sixth and seventh palsy probably could not occur independently on account of the close relationship of their nuclei. In the absence of pathological evidence he thought the condition was most likely a degenerative one involving the nuclei of the affected nerves and that it was probably toxic in origin.

The views of Moebius were, for the most part, accepted, but by no means unanimously; several earlier /

earlier writers were nearer the mark than he.

Mauthner (1885) was one of the first to propound the idea of an aplasia of the nuclear cells. Chisolm (1882) thought the lesion in the third case of this series was "a local aplasia of the grey matter in the medulla," while Hirschberg (1887) thought an aplasia of the cranial nerve nuclei was the cause of these congenital palsies.

A revulsion of opinion in favour of the aplastic conception followed the able review of Kunn (1895) on the subject of congenital ocular palsy in which he sharply differentiated congenital and acquired types and considered the former to be due to an aplasia of the corresponding nuclear cells. This hypothesis appeared to be confirmed by the pathological evidence afforded by Heubner's typical case in 1900. The contradictory evidence presented by Rainy and Fowler's atypical case a few years later tended to confuse the issue, but the agenetic view continued to prevail pending further evidence. This was long denied and not until 1931, when Spatz and Ullrich's case with multiple palsies was described, was confirmation of Heubner's findings realised.

Alajouanine, /

Alajouanine, Huc and Gopcevitch, in 1930, described four cases in young children from the Salpêtrière with bilateral sixth and seventh palsy and club foot. They were unaware of the association of club foot having been recorded before and considered that these cases constituted a new congenital syndrome. In reality nine of the cases of the present series previously recorded had club foot, six of them being bilateral. As a result of the claim of Alajouanine et. al. to have described a new syndrome most of the subsequent cases published have had club foot. This tendency to segregate the cases presenting this anomaly is unnecessary and undesirable as it tends to complicate the picture.

Those cases of paresis of the orbiculares palpebrarum muscles complicating ophthalmoplegia externa have not been included in this review. Mendel's hypothesis, in so far as it concerns the palpebral muscles, is still unverified; he contended that the motor fibres to these muscles originate in the third nuclei. Hughlings Jackson (1893) was the first to record the association of paresis of the orbiculares palpebrarum muscles and ophthalmoplegia externa, he described three cases who were not relatives. In /

In the following year Gazépy (1894) published an account of two brothers who exhibited similar characters which were congenital, in this instance there was a strong hereditary taint. It is now generally recognised that congenital and hereditary ophthalmoplegia externa are frequently accompanied by paresis of the orbiculares palpebrarum muscles; the familial type usually makes its appearance in adolescent or adult life.

Thomas (1898), Cabannes (1900) and Falloux (1909) reviewed the cases of congenital facial palsy then extant. One has found, however, that they failed to include several of the cases of this series; further, these reviews consisted chiefly in detailed accounts of the individual cases, the number being too small at that time for such an exhaustive study of the clinical and other features as is now being undertaken. Fry and Kasak (1919), Kirby (1923) and Bonar and Owens (1929) published very sketchy and superficial reviews on the subject of congenital facial diplegia; many cases were omitted by these authors, while their remarks about the features of the condition were very general. Neurath (1907) and Zappert (1910) reviewed the available /

available pathological evidence regarding congenital cranial nerve palsies in general, the cases were few and varied, and their conclusions were, therefore, indefinite.

AETIOLOGY.

Familial Incidence. In four instances two or more members of a family were affected, Thomas's (1898) two cases were brothers and Köster's were also brothers, while Cadwalader's (1922) elder girl was said to have a brother similarly affected. Beetz's three cases were siblings and a fourth, who died aged fifteen months, was said to have had a mask-like face from birth. There was a family history of congenital defects in Thomas's cases, also in Lennon's (1910) elder case and that of Fry and Kasak. Though a family history of congenital deformities is not mentioned in any of the other cases it is probable that in some of them this may not have been a matter of careful enquiry.

It is of interest to note that the siblings of Thomas, Köster and Cadwalader all belonged to the small group of pure facial diplegia. Consanguinity was a feature of the Beetz family, there had been two instances of intermarriage in the previous three generations and the family lived in an isolated valley of the Black Forest where intermarriage is notoriously frequent. It is well to recall here that /

that none of the three cases of this family were typically affected. It is evident then that there is a definite tendency for the condition to show a familial incidence.

Of congenital eye muscle palsies in general, ptosis, the commonest, has strong hereditary characters, the dominant being more frequent than the recessive type. The hereditary occurrence of lateral rectus and of superior oblique congenital palsy has been recorded, and also of ophthalmoplegia externa. Most of the hereditary instances of ophthalmoplegia externa, however, are acquired in youth or adult life and are of the dominant type; they thus belong to the neuro-degenerative disorders which are so often of a hereditary nature.

Toxic, Vascular and Mechanical Theories.

Syphilis was for long suspect in this condition as is often the case in obscure maladies, but it has ceased to be considered as a factor. The Wassermann reaction was weakly positive in only one of the eight cases tested, and that is of no significance. Alcohol and other toxic agents were thought by some to be the harmful factors. Oppenheim thought that vascular defects were the most probable cause of the nuclear agenesis, but his /

his views were purely hypothetical.

Mechanical influences of an extraneous nature were frequently incriminated in this as in many other congenital anomalies. Some thought that pressure on the brain, arising from disturbances in its immediate surroundings, might prove to explain the nervous phenomena.

The Relation of the Syndrome to Lymphangiectatic Oedema. The speculations of Ullrich of Essen, published in connection with his case in 1930, are worth recounting on account of subsequent experimental work on mice to be described later. The neck of his patient was grossly swollen at birth and the right hand and both feet were also swollen; the swellings of the limbs subsided slowly, disappearing in the second year. In addition to the pterygium colli which stretched from the ear to the acromion process on either side, there was bilateral ptosis, facial paresis and hypoplastic mammae. Ullrich regarded this as a case of lymphangiectatic oedema, an extremely rare condition which was thought to be the result of local circulatory disturbances in foetal life. He quoted the cases of /

of Kobylinsky (1883), Funke (1902), Fromme (1905) and Erlanger (1914) - the only others known to him - in which the swellings subsided in a few weeks or months after birth. Kobylinsky's case had pterygium colli and bilateral ptosis and Funke's pterygium colli, a mask-like face which was probably due to facial paresis and aplastic mammae. Fromme's case also had pterygium colli, while Erlanger's, in addition to this same feature, had epicanthus and a flat nose bridge - there had been oedema of the face in this case, particularly in these situations.

It is well to recall that in this series of cases, in addition to the case of Ullrich with pterygium colli already mentioned, that of Schmidt with multiple cranial nerve palsies exhibited pterygium axillare on the side of the pectoralis defect.

Ullrich was struck by the association of the rare conditions of lymphangiectatic oedema, skin folds, muscle defects and mobility disturbances in the field of the cranial nerves which these cases show. He concluded that all these conditions, sometimes associated, were most probably due to some abnormal /

abnormal process occurring in the early weeks of foetal life and he inclined to the view that pressure effects resulting from amniotic disturbances in the fifth-ninth weeks were the most likely cause.

An interesting sequel to these speculations of Ullrich has emerged from his own pen in the recent voluminous German Handbook of Neurology edited by Bumke and Foerster (1936). He discusses the embryological studies of Kristine Bonnevie (1934), Professor of Zoology at Oslo, and he considers that her observations on the aetiology of the congenital deformities of the Bagg-Little mouse tribe furnish an explanation for these congenital anomalies in man which he previously believed must have a common cause.

The /

The Observations of Bagg and Little on the
Development of Congenital Anomalies in
their Special Mouse Tribe.

It is imperative at this stage to consider the evidence presented by zoologists, working with a special strain of mice, before attempting to apply it as a possible explanation of anomalies in the human subject. In 1921 Bagg and Little (1924), in the United States, treated some mice with light doses of unfiltered X-Rays on five consecutive days, for several years these mice had been inbred as a single line. No abnormality appeared in the direct progeny and the two litters which were the ancestors of the abnormal mice were not born until thirteen and fourteen weeks respectively after exposure of the parents. This suggested that a true temporary sterility had been caused, and an alteration in the germ plasma which was responsible for the inherited defects of the off-spring. The descendants of these mice were affected with congenital eye and foot abnormalities, recessively inherited characters which were never found in over 2000 controls. Bagg (1923) demonstrated, through his ingenious experiments on living embryos in utero, that the foot anomalies //

anomalies were preceded by the formation of a blister-like "bleb" which raised the epidermis of the foot in a localised area; this occurred in 12-13 day embryos. On the 14-15 days blood escaped into these blebs forming blood clots which acted as a mechanical hindrance to normal development of the underlying tissues. He attributed these formations to some hereditary anomaly of the lymph vessels. Their extent and location determined whether the resulting foot defects were to show either congenital amputation, clubbing, hypodactyly or syndactyly. The eye abnormalities, which were the most constant feature, were preceded by similar formations, the haemorrhagic ones being known as "blood spectacles"; they varied greatly in degree, but consisted essentially of malformations of the cornea and adnexa, the deeper structures of the eyeball were usually unaffected.

Bagg and Little were unable to separate the various anomalies from each other by breeding experiments, which suggested to them the probability that genetically the whole group of anomalies represented different manifestations of the same hereditary /

hereditary character, but the nature of this remained obscure.

The Observations of Bonnevie on the
Bagg-Little Mice.

In 1930 Bonnevie acquired six mice of the Bagg-Little tribe, all with eye and fore-foot abnormalities. She examined 1000 individuals, 700 of which were embryos at stages of development varying from 1 mm. in length up to the time of birth. Immediately after killing the mother the live embryos were examined under the binocular loupe to ascertain the existence of "blebs" and their localisation. They were then fixed and re-examined and if desired serially sectioned. I will now describe Bonnevie's observations and her interpretation of them.

In 137 embryos below 7 mm. not a single bleb was found, but in those of 7-8 mm. they were present in a majority; they first appeared in the dorsal neck region. A statistical survey of the location of embryonic blebs in correlation with the stage of development shows that there occurs a gradual displacement /

Embryonic blebs, in percentage of the material investigated, grouped according to their localization and to the stage of development of the embryos.

[illegible]

displacement of the blebs from their place of origin in the neck, along the median dorsal surface, and also around one or both sides of the embryo. During this displacement the bleb fluid is seen to follow concavities of the embryonic surface, and it may finally find characteristic resting places, especially in the furrow surrounding the eyes or on the back of the nose. A preliminary resting place is often found in a concavity across the shoulder region; the fluid sooner or later continues its course down one or both sides to the tip of the fore feet or proceeds along the back and becomes concentrated on its hind part. From the latter situation part of the fluid may pass along the tail and escape from its tip, while part may remain on the back until resorption occurs, or occasionally continue its way down the hind limbs.

A characteristic feature of the abnormality is seen in minute "border blebs" which often appear - in embryos 8-10 mm. in length - at the tibial border of the hind limbs, and occasionally on their fibular border or on the fore-limbs. They arise simultaneously with those of the head and earlier than those of the back. Thus they seem to develop directly /

directly from the original head blebs, minute quantities of fluid passing from the neck region along the side of the lateral fold and concentrating at the border of the leg. Drop-like blebs were occasionally noted at the ventral side of the body, it is not surprising that such minute amounts of fluid moving under the epidermis often escaped observation. While most of these border blebs are resorbed without leaving any trace, others cause characteristic abnormalities of the hind feet.

Moving bleb fluid seems to cause no disturbance of the embryonic development, but when the fluid concentrates at a resting place its pressure may cause a breaking down of blood capillaries forming a haematoma; this was actually observed taking place during the examination of some of the living embryos. Such high pressure blebs may mechanically obstruct developmental processes, especially those of the eyes and feet, thus causing persistent abnormalities.

A thorough investigation of the bleb structures shows that the fluid lies below the very thin embryonic epidermis. The displacement of blebs along the embryonic surface seems to be governed by purely /

purely mechanical forces, represented above all by the elasticity of the epidermis forming the bleb roof which distributes the fluid in the direction of least resistance, that is, along the concavities of the embryonic surface.

A preponderance of left sided abnormalities, especially of the fore-feet, is thought to be due to the right-sided spiral curling of the embryonic body which still exists at stages when the location of the bleb fluid is taking place. Such curling may cause a difference of tension in the epidermis, especially in the shoulder region where the twisting of the body is most pronounced. The location of blebs and abnormalities was also found to be influenced by the varying embryonic surface moulding of different out-crossed races of mice, each of which had a characteristic distribution of defects.

Bonnevie says - "The bleb fluid takes its origin in the medullary tube, and is expelled in embryos 7 mm. in length, through the foramen anterior, a pear shaped opening existing for a short embryonic period in the anterior part of the roof of the myelencephalon. The expulsion of cerebrospinal fluid through this opening /

opening is, as shown by Weed (1917), to be considered as a normal occurrence. In this case, however, the quantity of expelled fluid is abnormally high."

Bonnevie concludes that "while the hereditary abnormality of excessive fluid formation is caused by one main recessive gene, other genes, each of which is responsible for specific features of the embryonic surface curvature, modify the specificity of its manifestation."

The Histological Observations of Plagens
on the Formation of the Deformities
of the Bagg-Little Mice.

Plagens (1933), whose material was mostly histological and much less extensive than Bonnevie's, was unable to confirm her observations on the origin of the "bleb" fluid in the dorsal neck region. He observed that the appearance of the blebs, some of which formed haematomas, was soon followed by thrombosis in the adjoining vessels. He regards the thrombosis as the sole cause of the deformities. Bonnevie does not agree with this view; she holds that, although thrombosis frequently considerably augments /

augments the mechanical effect of the blebs or haematomas, its occurrence is not an essential factor in the production of the abnormalities.

Weed's Experiments on the Establishment
of the Circulation of the Cerebrospinal
Fluid.

A study of Weed's classical monograph on "The Development of the Cerebrospinal Spaces in the Pig and in Man" shows how the cerebrospinal fluid which, according to Bonnevie, forms the blebs in the Baggett-Little mice, might reach the epidermis.

Weed was the first to demonstrate the existence of a temporary area of differentiation in the anterior half of the rhombic roof, the entire existence of which is confined to the second foetal month. As will be seen later, this area is of great importance, as, through it, the initial extension of cerebrospinal fluid from the cerebral ventricles into the periaxial mesenchyme occurs. Weed called this area the "Area Membranacea Superior Ventriculi Quarti." Differentiation of the cells of /



of the upper part of the roof begins in the pig embryo at the 8 mm. stage; by the 13 mm. stage the area has become sharply differentiated and consists of a permeable membrane of mesenchyme cells one layer thick. Its maximum differentiation occurs at the stage of 18 mm., is maintained through several mms. and then undergoes final retrogression. Its final obliteration, due to the caudal growth of the cerebellum and the enlargement of the chorioid plexus of the fourth ventricle has taken place in embryos of 30 mms. A similar area of differentiation, the "Area Membranacea Inferior Ventriculi Quarti" occurs in the lower half of the rhombic roof. Differentiation of this area is first seen at the 15 mm. stage and it proceeds slowly until 18 mms. is reached; it then proceeds with great rapidity in the next few mms., soon involving the whole inferior half of the rhombic roof to form a complete membrane consisting of a single layer of cells unlined by ependyma. This membrane persists, whether it does so as an intact membrane or whether it becomes perforated to form a foramen of Magendie is still a matter of controversy.

These /

These structural changes occurring in the roof of the fourth ventricle were those observed in the pig embryo, but Weed showed that almost exactly comparable changes occur in the human embryo at corresponding stages of development. The time of formation, maximal development and regression of the superior area, coincides almost exactly in the pig and in man. He thinks the existence of this temporary area probably occurs in all mammals.

Through the agency of dyes in true solution, with which he replaced the fluid of the ventricles and spinal canal under normal pressure, Weed demonstrated that an outflow of cerebrospinal fluid through the superior membraneous area commences in the 14 mm. embryo and coincides with the beginning of villous tufting in the chorioid plexus of the fourth ventricle. The formation of the chorioid plexus would seem to indicate the beginning of active cerebrospinal fluid production, leading in turn to a raised intra-ventricular pressure and the initial filtration of fluid through the already almost fully differentiated superior membraneous area. Until the 18 mm. stage is reached the escaped fluid remains localised in the peribulbar mesenchyme /

mesenchyme, but at this stage, coinciding with the formation of the chorioid plexuses of the third and lateral ventricles, there is a further sharp increase of cerebrospinal fluid production and an outflow of fluid begins through the inferior membraneous area also. Owing to the free elaboration of cerebrospinal fluid now taking place the further peri-cerebral spread of fluid occurs very rapidly, and the filling of all the periaxial mesenchymal spaces is completed in embryos of about 26 mm. The circulation of the cerebrospinal fluid is not established until the embryo reaches a stage of 23 mm. when it begins to pass into the venous sinuses of the dura mater. Weed showed by demonstrating the passage of dye through the cytoplasm of the membrane cells that the transference of fluid occurs by filtration determined by differences in pressure.

The mesenchyme, which forms a fragile syncytial network of rather small mesh, is quite thin between the anterior membraneous area and the overlying epidermis. When discussing the earlier stages of extramedullary fluid spread Weed says "the outer layer of the arachnoid is not at all differentiated, here the barrier to the fluid is the blastemal condensation of mesenchyme destined to form the dura-periosteum. In some areas, /

areas, however, this has not yet occurred, this is shown particularly well in the region of the roof of the fourth ventricle, where the epidermis offers the only barrier to the passage of fluid from the pericerebral spaces." In the later stages when the outer layer of the arachnoid is beginning to appear as a mesenchymal thickening, the fluid is confined strictly within the immature arachnoid membrane.

Ullrich's Analogy Between this Syndrome
and the Anomalies of the Bagg-Little Mice.

As might have been expected, Ullrich, who had already identified lymphangiectatic oedema with muscle defects and palsies in the field of the cranial nerves, quickly saw the possible significance of Bonnevie's discoveries when applied to the human subject. He thinks that they offer the likely explanation for many developmental disturbances, those found in this syndrome being the most typical combination, and that a solution is offered which accounts for the many apparently irreconcilable anomalies in what has always been a completely unintelligible clinical picture. Ullrich does not think that Plagens' inability to confirm Bonnevie's observations on the medullary origin of the bleb fluid need cause one to doubt them. He considers that the association of cranial nerve aplasias, as found /

found in this syndrome, with malformations which resemble those of the Bagg-Little mice so closely, strengthens Bonnevies argument in favour of the cerebral origin of the fluid. He thinks that the location of the primary bleb, over that part of the medulla most frequently the site of nuclear hypoplasia, indicates that such agenesis is caused by the pressure of the overlying vesicle at a definite and crucial time in development. Also, that the less frequent hypoplasia of the nuclei in the hinder part of the mid-brain, and the distal part of the medulla, are produced through the same agency.

The unilateral type of facial palsy, unaccompanied by other cranial nerve palsies, but complicated by hypoplasia of the petrous temporal bone and inner ear and also of the auricle, is accounted for by the passage of fluid to the side of the head. Further progress in that direction would lead to the orbital depressions whence for physical reasons its dissipation is precluded. Ullrich thinks that the flattening of the root of the nose so often seen in these cases is due to its influence, also epicanthus and absent lachrymal caruncles. The local /

local pressure of the fluid, he believes, could also account for eye muscle defects. Upper trapezius and sterno-mastoid defect and severe involvement of the deep neck muscles are rare, but held to be due to neck blebs; while the further passage of fluid in that direction may cause hypoplasia of the clavicle and the attached clavicular part of the pectoralis major. Its final resting place, however, at the side of the chest, causes defective development of the corresponding part of the pectoralis major and of the minor, and sometimes more extensive hypoplasia involving the ribs. To the pressure of fluid displaced caudally to the shoulder region he attributes trapezius defect and that of other scapular muscles. He notes how muscles like the deltoid which occupy convexities escape. Sprengel's deformity, due to an arrest of the normal descent of the scapula occurring during the second month, he thinks is most likely due to the presence of this fluid also. The deformities of the hand and fingers which occur in this syndrome and harmonise "to the last detail" with the fore-foot anomalies of the mice point to a similar origin. He also draws a parallel between the relative infrequency of hind limb /

limb anomalies in the mice and the absence of muscle defects and deformities in the legs and feet of man, but he makes no mention of the club foot so frequently encountered in this syndrome.

Ullrich believes that such anomalies as uncomplicated muscle defects and isolated finger deformities may, of course, have quite a different foundation.

In discussing the differential diagnosis of congenital cranial nerve palsies in which, - in the case of some nerves - either or both ends of the peripheral neurones may be affected by overlying vesicles, the point is made that disturbances in the nuclear field can only be diagnosed with complete certainty where the palsies are bilateral and multiple, the most typical being a combined bilateral sixth and seventh palsy. Owing to their close proximity the damaging of a single nucleus by a pressure effect as postulated is improbable, and, Ullrich believes, in conformity with this assertion, that bilateral seventh palsy alone cannot be nuclear. The great difficulty of arriving at the cause in many cases of isolated eye muscle palsies is emphasised, but adnexal /

adnexal anomalies suggest a defect of external ocular muscles resulting from orbital bleb formations.

Discussion.

The hypothesis of Ullrich is both absorbing and suggestive. It appears to offer a logical explanation for the very widespread and varied anomalies which occur in this syndrome and explains the absence of internal anomalies. Further, a single disturbance accounts for all the anomalies, a fact which always commands attention in clinical work. A close examination of the evidence, however, has convinced me that Ullrich in his enthusiasm has assumed too much, and is quite unjustified in saying that the mode of origin of the anomalies of this syndrome has been proved through the agency of the Bagg-Little mice.

One regrets that Bonnevie's work has not as yet been confirmed, but I am told by zoologists that her reputation stands high and that her work is always regarded as being very sound. I find it difficult to believe that her uniform observations on /

on 700 live embryos of all sizes could have been entirely false. It seems more likely that Plagens, working with a much smaller number and with dead embryos and histological sections, was unable to see the earlier bleb formations and thus failed to trace their origin. Along with Ullrich I am inclined to accept Bonnevie's work, but, in view of the lack of confirmation and of Plagens' inability to do so, I would rather display more caution than he and say that, although the mode of origin of the bleb fluid is probably that described by Bonnevie, the matter requires further investigation and proof.

I agree that the evidence in favour of a similar origin of the deformities of the Bagg-Little mice and the patients of this syndrome is very suggestive, but I am dissatisfied with Ullrich's explanation of the pathogenesis of the nuclear defects. I do not think it is possible for a primary neck bleb overlying the medulla to cause the nuclear aplasia which Ullrich believes is the case. As Weed has demonstrated so beautifully, the cerebrospinal fluid filters through the permeable membranes of the rhombic roof by virtue of a higher intra- than extra-medullary pressure. Therefore, an accumulation of fluid over the rhombic roof could not press it against /

against the floor of the medulla, thus injuring the motor nuclei at a "critical stage of their development." An excessive production of fluid in the early stages would lead to its peri-bulbar accumulation, the resulting increase of pressure would, in turn, raise that in the cerebral ventricles and this might interfere with the development of para-ventricular cell masses. Granted that this might occur, why the selectivity? The fluid pressure would, of course, be equal on all the ependymal surfaces of the cerebral ventricles. It seems probable that the very superficial position of the sixth and seventh nuclei at the stage of development in question could be the explanation for their more frequent involvement. One wonders whether this is not a hair-splitting argument when considering the 14-23 mm. embryo in which the nervous and other tissues are so soft, but I cannot think of any other way in which increased fluid formation could exert an injurious effect on the tender nervous tissues of the embryo.

The raised pressure of the fluid in the cerebral ventricles and the peri-axial mesenchyme would, /

would, of course, only be possible between the 14 mm. stage, when the first chorioid plexus forms, and the 23 mm. stage, when the peri-axial fluid begins to be re-absorbed into the circulation via the venous sinuses, and the circulation of cerebrospinal fluid becomes established. In the case of the human embryo the time taken to grow from the 14 mm. to the 23 mm. stage is about one week.

I believe, since the ease with which the fluid can reach the subepidermis has been demonstrated, that only a slightly excessive production of cerebrospinal fluid would be likely to cause an accumulation of fluid in that situation. Such an excess occurring in the first week of its active formation would pass along the paths of least resistance, which, as shown by Weed, lead to the subepidermal region overlying the fourth ventricle. From that situation the accumulating fluid is displaced subepidermally, according to Bonnevie, by the tension of the overlying epidermis on the convex surface. An excess of cerebrospinal fluid formation has been postulated, but knowing how easily the rate of flow is influenced in later life, the possibility of such an occurrence at this /

I wrote to them but I have again been disappointed. I intended to investigate the condition of the motor cranial nuclei as described already. I believe that, if nuclear hypoplasia were demonstrated in this way, the analogy between the mice and the patients of this syndrome would be close enough to make a similar pathogenesis almost certain; and if we accept Bonnevie's explanation of the origin of the bleb fluid it has been elucidated in the case of the mice.

Without the valuable evidence which an examination of the brain stems of the Bagg-Little mice would have afforded, one cannot draw definite conclusions, but a study of the problem has led one to the view that Ullrich's hypothesis of the pathogenesis of the anomalies occurring in the syndrome under review is the most rational one so far propounded, and has the merit of being based on experimental embryology and comparative pathology.

Ullrich's inclusion of lymphangiectatic oedema into the symptom complex under review, before he knew of the animal experiments, is interesting; from the latter he concludes that there is no doubt about its origin, but I think this an unwarranted claim for it is /

is no more than suggestive. The blebs, in their final situations, were frequently still present when the Bagg-Little mice were born. It was chiefly the paresis of the cranial nerves which led him to associate the conditions, but these were unlike those under review and, apart from Ullrich's case, none of this series had lymphangiectatic oedema. The question of this association must remain open until further evidence is forthcoming.

A consideration of the site of production of the various cranial nerve palsies seems desirable. Ullrich's conditions for the postulation of a nuclear origin are fundamentally correct, but one feels that some latitude should be allowed for occasional exceptions. Of the sixty-one cases of facial diplegia, it was combined with abducens palsy in forty-five, this being bilateral in all except two cases. In one of the unilateral cases - the second case of Beetz - the palsy was only slight, but there was also ptosis and trigeminal paresis: this multiplicity of lesions in conjunction with the familial incidence goes far towards proving that nuclear facial diplegia does occur independently of /

of sixth palsy occasionally. Conversely, the case of Phillips, Dirion and Graves, already quoted, shows that hypoplasia of the sixth pair of nuclei can occur without implication of the adjacent facial nuclei.

One concludes, then, that the cranial nerve palsies in the cases of this series are of nuclear origin, with the possible exception of some of those exhibiting pure facial diplegia.

The striking differences of the "pure" and "complicated" facial diplegia group have already been alluded to. I believe that ear deformities, which are much commoner in the pure group and are prone to be accompanied by deafness, indicate that the diplegia may be due to local pressure on the developing temporal bones by displaced fluid, as suggested by Ullrich in connection with the unilateral type. Of the ten cases of pure seventh palsy there was insufficient detail in two, four of the other eight had deformed ears, and two of these were deaf; of the four without external ear deformity three were too young to assess the acuity of hearing and the fourth was deaf. Deafness was never noted in /

in the complicated group of fifty-one cases, which suggests that it is significant. The possibility of birth trauma, raised by Rainy and Fowler's case, must be kept in mind where there are no auricular or other stigmata.

Mental defect was a feature in a significant number of patients, it was always associated with multiple cranial nerve palsies which suggests the occurrence of a widespread hypoplasia of nervous elements in such cases. Cortical hypoplasia is one of the principal characteristics in most types of amentia.

The suggestion of Ullrich that some of the ocular palsies may be due to muscle defects caused by the orbital blebs, is reasonable. Eye muscle defects have been demonstrated on numerous occasions in cases without facial paralysis. I think that the symmetry of the ocular palsies and the fact that ptosis is unusual in these cases - which would not be so if the cause were local - point to a central origin. There can be little doubt that the club foot which occurred in one third of the cases of this syndrome must be caused by the same process as the other anomalies. The type of deformity corresponds with the position of the fluid /

fluid vesicles on the hind limbs of the mice as shown by Bonnevie. This suggests its pathogenesis and brings this feature into line with the others of the syndrome.

I have recently had the pleasure of a talk with Professor Müller, the geneticist, who is working in the Department of Genetics in this University. He has discussed the pathogenesis of the anomalies in the Bagg-Little mice with Professor Bonnevie, whom he knows very well, and for whom he has the highest regard. He sees no reason to doubt her observations regarding the experimental production of mutations. He informed me that the harmful effect of rays on the chromosomes of the germ plasm is in proportion to the dose and that it is cumulative; thus a large number of very small doses which individually might be harmless would, in the aggregate, damage the chromosomes. In the experimental animal such damage, if it be severe, leads to partial sterility and a high incidence of intra-uterine death. He believes it possible that in future generations of the human subject some of the descendants of those who /

who have been exposed to X-Rays or radium may exhibit mutations. This is a disturbing thought, for, terrible as was the fate of many of the pioneer roentgenologists, the appearance of mutations in ones descendents, possibly such as those encountered in this syndrome, would be even more distressing. Let us hope and pray that we are not unwittingly inflicting irreparable harm on the germ plasm which is our heritage and of which we are the trustees.

Conclusion.

There can be little doubt that the association of nuclear defects with malformation of the limbs, etc., in such a high proportion of the cases of this rare congenital syndrome, shows that they must have a common cause. Bonnevie has shown how the closely analagous deformities of the Bagg-Little mice are produced, and it is probable that those of the patients under review, as well as numerous other congenital malformations, are produced in the same way. The absence of the valuable evidence which the brain stems of the Bagg-Little mice would have afforded is to be regretted. A careful study of Weed's monograph has shown how an excess production /

production of cerebrospinal fluid in the first week of its formation could cause both a hypoplasia of nervous elements and the structural defects of the limbs, etc., which are encountered in this syndrome.

SUMMARY.

An exhaustive review of the literature on the subject of congenital facial diplegia has been undertaken. Since the number of cases has become large enough to make it worth while this is the first time the clinical features of the condition have been analysed. A well defined clinical picture has emerged as a result of this study.

I have called the condition "The Congenital Facial Diplegia Syndrome" which appears to be the most appropriate designation. It emphasises the salient feature and implies the occurrence of a number of other characteristic congenital anomalies.

A typical case, an infant which is still under observation, has been recorded.

The incidence of the principal anomalies is as follows:-

Brain.

Facial diplegia	61 cases
Abducens palsy	45 cases
(bilateral 43. Convergent strabismus 23)	
Ophthalmoplegia /	

Ophthalmoplegia Externa, bilateral (Partial 14)	15 cases
Ptosis, bilateral	6 "
Lingual Palsy (bilateral 10)	18 "
Mental Defect	6 "

Major deformities.

Club foot (bilateral 16)	19 "
Deformities of arm and hand (bilateral 2)	13 "
Pectoralis muscle defect	8 "

Minor deformities.

Ear malformation	8 "
Epicanthus	6 "
Hypoplastic lachrymal caruncles	3 "
Bifid uvula	2 "

The facial palsy has a characteristic distribution when incomplete, the peri-oral muscles being the least affected and usually the only ones capable of any movement. No other type of facial palsy has such a distribution. The distribution is as follows:-

No. of cases with sufficient data	-	56
Complete facial diplegia	-	20
" upper " palsy	-	21
" lower " "	-	1
Complete /		

Complete unilateral facial palsy	-	11
No quadrant completely paralysed	-	10

Pathological data is available in only three of these cases. The basis of the cranial nerve palsies is an aplasia or hypoplasia of the relevant nuclei, with a consequent lack of development of the nerves and muscles connected therewith.

A historical sketch of the prevailing views with regard to the condition since it was first described has been given.

The aetiology, which is still a matter of speculation, has been discussed at some length.

There is a tendency for the condition to be familial.

Many views about the aetiology have been expressed but, until recently, none of them has had any foundation. Lately, however, Ullrich has been attracted by the close resemblance of the limb and eye malformations of these patients to those of a special /

special experimental strain of mice and he thinks that the aetiology in the two species is probably similar. Bonnevie has shown that the subepidermal "blebs" which precede the lesions in this special mouse strain arise in the dorsal neck region in early embryonic life. They are mechanically displaced to their final situations by the elasticity of the epidermis, the direction of displacement and the final location at which the permanent deformities are produced is determined chiefly by considerations of surface contour. Bonnevie assumes that the fluid is, in fact, cerebrospinal fluid and she justifies this statement by quoting the work of Weed.

A careful study of Weed's monograph on "The Development of the Cerebrospinal Spaces in the Pig and in Man" has shown how, during the first week of active cerebrospinal fluid formation by the chorioid plexuses, the surplus fluid in the event of an excess would be likely to take the course demonstrated by Bonnevie.

Ullrich's explanation of the possible mode of production of the nuclear aplasias by the pressure of the overlying primary neck bleb, at a critical stage /

stage of development, is untenable for reasons which have been given. I have endeavoured to explain how an excess of fluid might damage the developing nuclei. The attempt and failure to procure some of the special experimental mouse strain has been referred to. It was felt that the demonstration of an aplasia of the nuclei in the brain stem would have afforded valuable confirmatory evidence of Ullrich's hypothesis. Conversely, a normal state of the nerve centres would have rendered it untenable and thrown the mode of origin of the congenital cranial nerve palsies into complete obscurity once more.

One concludes that this most recent theory requires further support, but that it is reasonable. It has the merit of being based on comparative embryological evidence and of explaining the multiple widespread anomalies occurring in these patients which have hitherto baffled understanding.

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CASE ABSTRACTS.

Case No. 1.

v. Graefe. (1880).

Male. 20 years. Facial paralysis present from birth. Complete on left side. Slight on right side, the frontalis being paralysed.

Ocular paralysis. Bilateral abducens palsy, complete. No strabismus. The lower border of the left cornea is always on a lower level than that of the right.

Senses of smell and taste impaired.

Occasional petit mal attacks.

Muscular twitchings in both hands.

Case No. 2.

Harlan. (1881).

Male. 18 years. Paralysis of the face and convergent strabismus were noticed soon after birth and remained unchanged.

Facial paralysis. An expressionless face, inability to close the eyelids and epiphora were noted. The only movement was a slight drawing down of the corners of the mouth owing to platysma action.

Ocular paralysis. Bilateral abducens palsy, complete. Convergent strabismus of both eyes.

Case No. 3.

Chisolm. (1883).

Female. 35 years. Patient has never been able to close the eyelids and had a severe convergent strabismus of both eyes in childhood.

Facial paralysis. No wrinkling of the skin was noted on the face but, on trying to whistle, a few wrinkles appeared beneath the corners of the mouth and on the lower lip. Slight ectropion was present.

Ocular paralysis. Bilateral abducens palsy, complete. The severe convergent strabismus was corrected by operation in childhood, but the internal recti action was destroyed by it.

Aplasia of the lachrymal caruncles.

Hypermetropia was present.

Case No. 4.

Moebius. (1888).

Male. 50 years. Facial immobility was noticed in the first few days of life. Patient came under observation for a bilateral extensor palsy of the hands of nine weeks duration which was due to plumbism.

Facial paralysis. There was occasional dribbling of saliva from the corners of the mouth but no difficulty with eating or drinking. Moebius made special mention of the presence of horizontal frontal skin folds occurring with complete paralysis in that region. The only voluntary movement of the face was an outward movement of the left mouth corner. Only a few facial muscles reacted to faradism and galvanism, the mouth corners were weakly drawn outwards and downwards to both, the left more strongly than the right. The mentalis also reacted and the buccinators were easily stimulated.

Ocular paralysis. Bilateral abducens palsy, complete. No strabismus.

Brachial /

Brachial deformity. Syndactyly of the second and third fingers of the right hand.

Chronic conjunctivitis was a feature.

Case No. 5.

Schapringher. (1889).

Female. 8 years. Facial paralysis. The face was expressionless, there was no movement on laughing or crying. The left mouth corner could be drawn outwards and downwards.

Ocular paralysis. Bilateral abducens palsy, complete. No strabismus.

Lingual paralysis. The tongue was less easily moved than normally and deviated a little to the left on protrusion.

Trigeminal paresis. The lower jaw could only be moved towards the right, but not towards the left.

The following minor deformities were present:-

Epicanthus, hypoplastic lachrymal caruncles, protuberant glabella, bifid uvula, a sunken sternum and a deformed terminal phalanx of the left index finger.

The left eye was emmetropic and astigmatic, the right eye myopic.

Case No. 6.

Bloch. (1891).

Male. 9 months. Facial paralysis.

"Bilateral paralysis of the lower branches of the facial nerves."

Ocular paralysis. Bilateral abducens palsy.
Strabismus not mentioned.

Club foot. Talipes equino-varus, bilateral.

"Other abnormalities."

Case No. 7.

Fryer. (1892).

Male. 16 years. Facial paralysis. Complete
diplegia.

Ocular paralysis. Bilateral abducens palsy.
Strabismus not mentioned.

Brachial deformity. Congenital amputation of
the right hand and hypoplasia of the right arm.

Case No. 8.

Kirmisson. (1895).

Male. 7 years. Facial paralysis.

Complete diplegia.

Club foot. Talipes equino-varus, bilateral.

No other anomalies were mentioned as Kirmisson, who was an orthopaedic surgeon, was primarily interested in the club foot and mentioned the facial diplegia in connection with it. .

Case No. 9.

Procopovici. (1896).

Male. 18 years. Severe degree of facial paralysis from birth.

Facial paralysis. Palsy of nearly all the muscles of both sides of the face. Electric excitability almost abolished from the muscles of the face, especially the orbicularis and frontalis muscles. The muscles of the right corner of the mouth and of the chin and the right elevator of the alae nasi gave normal reactions.

No other abnormal findings were mentioned.

Case No. 10.

Procopovici. (1896).

Female. 7 $\frac{1}{2}$ years. Facial paralysis. Severe on both sides. The muscles about the corners of the mouth and the orbicularis palpebrarum had escaped.

Ocular paralysis. Bilateral abducens palsy, complete. Convergent strabismus of the left eye.

Epicanthic folds were present.

Case No. 11.

Schmidt. (1897).

Male. 6 years. Facial immobility and squint noticed at birth. The eyelids could not be closed. There was difficulty in sucking, the teat being taken further into the mouth than usual. There was no dysphagia. The child was thought to be mentally defective but was proved not to be as he grew older. Speech was imperfect and indistinct.

Facial paralysis. Inability to close the lips and occasional dribbling was noticed. Complete diplegia. No response of any facial muscles to faradism or galvanism.

Ocular paralysis. Bilateral abducens palsy. Convergent strabismus in both eyes.

Lingual paralysis. The tongue was very wrinkled, thinner and softer on the left side. There was often a slight arching more marked to the right side. The tip could not reach the upper teeth. On protrusion the tip deviated to the left and only reached to a little beyond the teeth. When eating food accumulated in the right cheek and he used a finger /

finger to push it back on to the tongue by pressing on the cheek. Speech was indistinct but understandable.

Pectoralis muscle defect. Flattening of the left side of the chest. Only the clavicular part of the pectoralis major was present, the pectoralis minor was absent. The left mammary gland and nipple were just seen. A web-like fold of skin stretched from the third rib to the middle of the upper arm.

Mild conjunctivitis was present.



FIG. 1. (Case 1.)

Case No. 12.

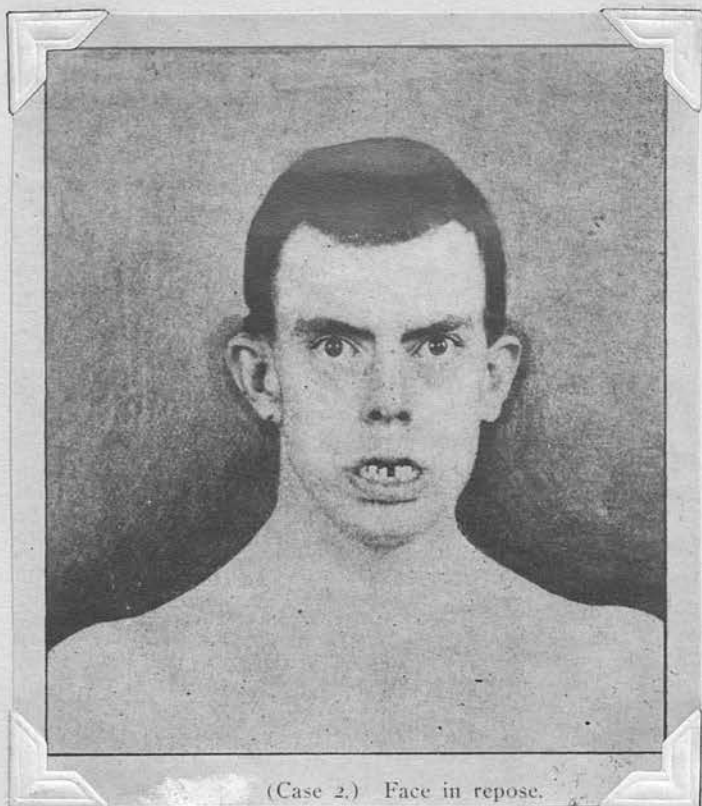
Thomas. (1898).

Male. 21 years. A brother of Case No. 13.

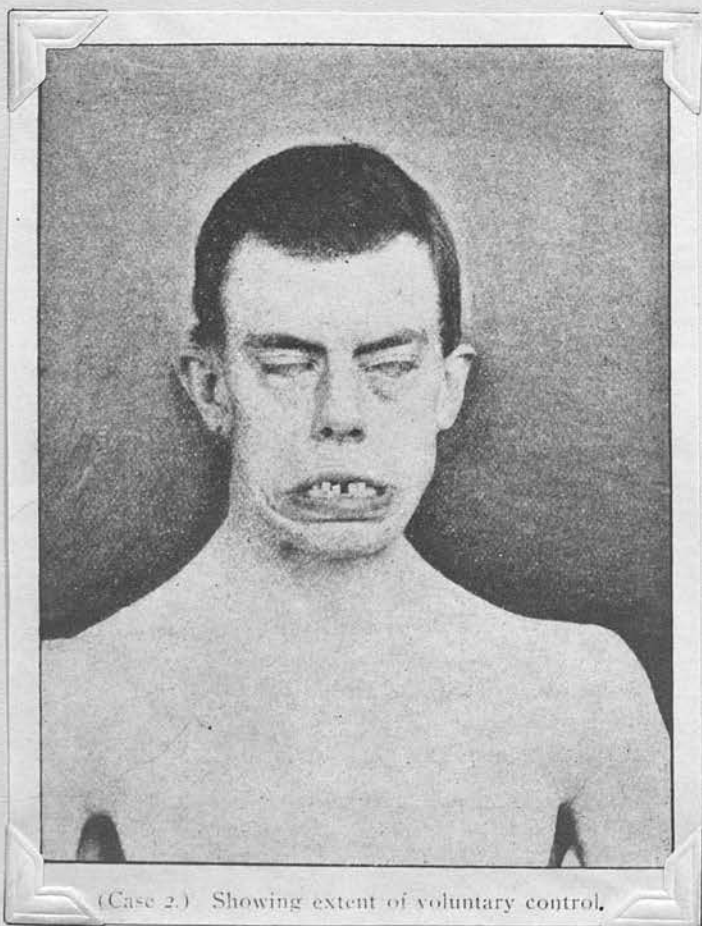
A sibling who only survived birth by two hours had a deformed foot. The mother's aunt had a child with one arm. Inability to close the eyelids when asleep and drooping of the lower lip were noticed soon after birth. There were no nursing difficulties. Mother thinks the patient's deafness was a result of measles in childhood but there had been no otorrhoea.

Facial paralysis. The face was quite expressionless, the mouth was open and there was a large everted lower lip. The only voluntary movements were an outward drawing of the right and a downward drawing of both mouth corners through platysma action.

Ear lobes slightly deformed. There was a severe degree of deafness on both sides.



(Case 2.) Face in repose.



(Case 2.) Showing extent of voluntary control.

Case No. 13.

Thomas. (1898).

Male. 19 years. A brother of Case No. 12.
Condition of face noted shortly after birth. No
nursing difficulties.

Facial paralysis. An expressionless face with
an open mouth and a large pendulous lower lip. The
mouth corners could be drawn down by platysma action.
The buccinator muscles had retained some power.
The only muscles which responded to electrical
stimulation were the above and the contractions were
diminished in intensity.

Ear lobes slightly deformed. Severe bilateral
deafness.

Case No. 14.

Heubner. (1900).

Male. 1 year, 7 months. Facial palsy from birth. Died of broncho-pneumonia. First sat up at sixteen months, had not begun to walk or speak. When asleep there was an interval of three mms. between the eyelids. Dribbling of saliva was troublesome.

Facial paralysis. Complete on the left side. On the right side the only voluntary movement was an outward drawing of the mouth corner.

Ocular paralysis. Bilateral abducens palsy. Inconstant convergent strabismus of one or other eye. On looking up the lower border of the right cornea was on a lower level than that of the left.

Lingual paralysis. The left half of the tongue was smaller than the right and its surface was furrowed.

An absence of tear secretion even during electrical stimulation was a striking symptom.

Patient was regarded as backward but not mentally defective.

Pathology, see text.

Case No. 15.

Bernhardt. (1901).

Male. 10 months. The abnormal appearance of the face was noted at birth. The infant could not suck.

Facial paralysis. Facial immobility, an ever-open mouth and an everted lower lip were the striking features. Epiphora was a notable symptom, while, during sleep, the eyelids were never closed. The only movement was an almost imperceptible one in the right lower lip. The muscles in that situation were the only ones that responded to electrical stimulation and they reacted feebly.

Case Nos. 16 & 17.

Koester. (1902).

Both males. Ages unknown. The patients were brothers.

Facial paralysis. Complete diplegia in both. Only the chin muscles could be stimulated electrically.

Absence of facial perspiration even with pilocarpine was an interesting symptom. Tear secretion was normal.

Ear deformity. Slight in both.

Case No. 18.

Decroly. (1902).

Male. 7 weeks. Facial immobility even on crying, an open mouth and inability to close the eyelids were noticed at birth. The infant was slow in learning to nurse, but after three days was able to do so. Dysphagia and nasal regurgitation were troublesome and the infant was soon weaned.

Facial paralysis. Complete diplegia.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial. Only lateral movements of the eyes seemed possible. As far as could be determined at this age the palsy appeared to affect those muscles supplied by the third nerves, while the lateral recti supplied by the abducens nerves had escaped. Owing to the patient's tender age these atypical ocular findings should not necessarily be regarded as accurate.

Mild conjunctivitis and dacryocystitis were present.



FIG. 2.



FIG. 3.

Case No. 19.

Taylor. (1902).

Male. 15 years. Had never shown any facial expression or movement, as an infant "would not have known he was crying except for the open mouth and the noise." At the age of five years all four limbs were said to have been paralysed but recovery soon took place.

Facial paralysis. The mouth was always open and the eyelids were never completely closed. Speech was indistinct, the labials not being pronounced. The only muscles showing slight voluntary movements were the risorius, the depressors of the angles of the mouth and the orbicularis oris.

Ocular paralysis. Bilateral ptosis, slight.

Paresis of soft palate which moved sluggishly. There was slight dysphagia.

Case No. 20.

Rainy & Fowler. (1903).

Female. 10 weeks. Forceps delivery. Died
of broncho-pneumonia.

Facial paralysis. Face immobile apart from
contraction of a few fibres of the right frontalis
muscle just above the extreme inner angle of the eye,
also of the right depressor anguli oris. The
electrical reactions were negative.

Pathology, see text.

Case No. 21.

Batten. (1905).

Child, 9 years. Was never able to suck.

Facial palsy from birth. First seen at two and a half years, unaltered since.

Facial paralysis. Partial palsy of both sides of the face, the right worse than the left.

Ocular paralysis. Bilateral abducens palsy. No strabismus mentioned.

Lingual paralysis. "Atrophy" of both sides of the tongue.

Case No. 22.

Gierlich. (1905).

Female. 14 years. Inability to nurse was noticed soon after birth. There was no dysphagia or nasal regurgitation. Immobile face from infancy. Treated for lues since the first year.

Facial paralysis. The mouth was open with dribbling of saliva from the corners. Speech indistinct, no lip sounds. Only facial movements were a drawing downwards and outwards of the mouth corners. Ectropion and epiphora were other features.

Ocular paralysis. Bilateral abducens palsy. Bilateral convergent strabismus, diplopia.

Lingual paralysis. The tongue lies on the floor of the mouth slightly curled with the tip towards the right. On protrusion it deviates towards the left. The left half is thinner than the right and wrinkled except near the tip.

Case No. 23.

Gützmann. (1905).

Male. 12 years. Suckling difficulty was noticed soon after birth and the child never laughed or cried normally. The appearance of the patient was reminiscent of myxoedema owing to the thick skin and swollen face which was most marked in the lips.

Facial paralysis. The face was smooth and mask-like, lip sounds could not be made. The only movements were those due to the risorius muscles.

Ocular paralysis. Bilateral abducens palsy, complete. No strabismus.

Brachial deformity. Right hand very hypoplastic, syndactyly of the fore and middle fingers and also the third and fourth to a less extent.

Club foot. Bilateral talipes equino-varus.

Mammary hypoplasia, bilateral.

Case No. 24.

Ziehen. (1908).

Male. 18 years. Forceps delivery.

Abnormalities present from birth. Rickets in infancy, also convulsions in the first two years. Retarded mental development in early childhood. Speech began at three and a half and walking at five. Later mental development normal.

Facial paralysis. Facial immobility very striking. Mouth always open, complete palsy of the lower face. The only movement possible was a very slight contraction of the orbicularis oculi muscles on attempting to screw up the eyes.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial, of severe degree. Both eyes could be lowered and converged and the left raised slightly. Bilateral ptosis of severe degree.

Lingual paralysis. Severe, the atrophy and palsy were worse on the left side. Constant fibrillary twitchings were observed.

Pectoralis muscle defect. There was, in this case, complete absence of sterno-costal part of left pectoralis major, the clavicular part and the minor were /

were poorly developed. Left mamma hypoplastic.

Forehead low with hair margin reaching unusually far down.

Case No. 25.

Collins. (1909).

Sex and age unknown. Facial paralysis. No details regarding severity or distribution obtained.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial, of severe degree. The inferior recti were the only functioning muscles.

Lingual paralysis. Left-sided.

Pectoralis muscle defect. Left-sided.

Case No. 26.

Lennon. (1910).

Male. 2 years. Abnormalities noticed at birth. Could not suck with his lips.

Facial paralysis. Complete diplegia.

Electrical reactions negative.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial, of severe degree. Movements in any direction only slight. Bilateral convergent strabismus, severe.

Club foot. Bilateral talipes equino-varus.

Diastasis of the abdominal recti muscles, of marked degree.

Case No. 27.

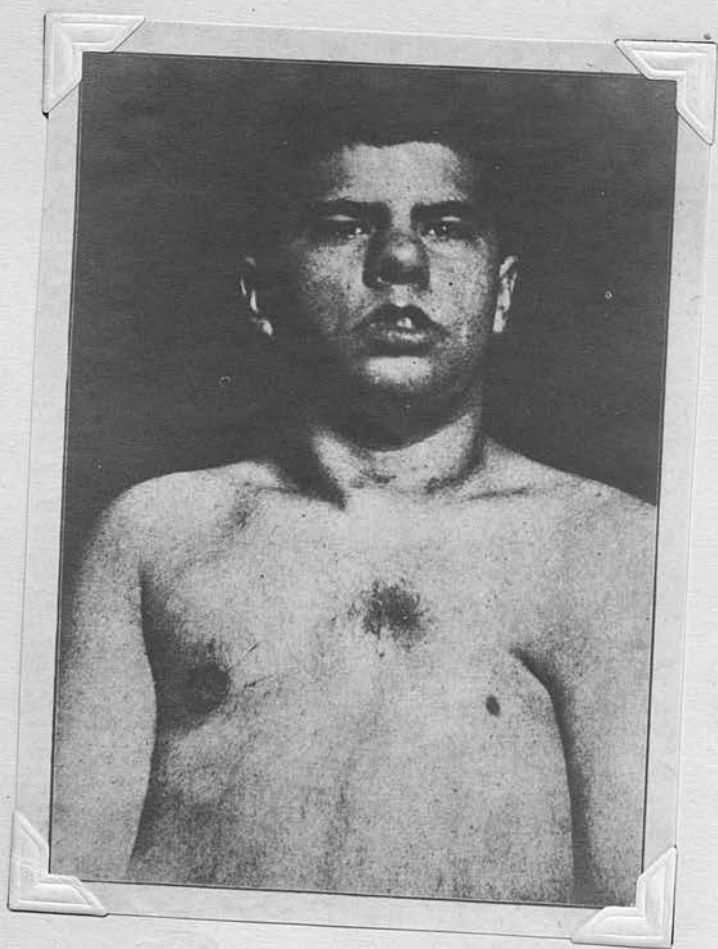
Lennon. (1910).

Male. 14 years. A cousin had hypoplasia of the right arm and hand. Club foot and strabismus and incompletely closed eyelids were noticed at birth. There was always some movement about the mouth.

Facial paralysis. Partial closure of the right eye possible on screwing up the face. On smiling there is "a peculiar and well marked grimace on the left and a somewhat different and lesser movement on the right." Electrical reactions corresponded to these movements.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial, of severe degree. Movements of the eyes very limited in all directions. Bilateral convergent strabismus, severe.

Club foot. Bilateral talipes equino-varus which has been rectified.



Case No. 28.

Peritz. (1912).

Male. c.20 years. Facial paralysis which appears to be of severe degree in the accompanying photograph. No details are given..

Ocular paralysis. None mentioned.

Pectoralis muscle defect, left-sided.

Mental defect, slight, and nervous instability.

Case No. 29.

Welde. (1912).

Female. 2¹/₂ years. Mother noticed day after birth that the right nostril was collapsed and the right mouth corner was higher than the left. Was unable to suck and had dysphagia. At four months mother took to clinic owing to the immobile face, the open mouth, the dysphagia and frequent squinting, also incomplete closing of the eyelids during sleep. Mother returned to clinic later because of slow mental development.

Facial paralysis. Complete diplegia. The skin of the face appeared stretched and the face atrophic, more so on the right causing facial asymmetry. Electrical reactions, slight response to galvanism of the orbicularis oculi muscles and those at the corners of the mouth.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial, of severe degree. Only slight movements, mostly convergent, were possible. Convergent strabismus in both eyes.

Lingual paralysis. Asymmetry and hypoplasia more marked in the front half and worse on the right side. The tongue is never protruded. Dysphagia still an occasional symptom.

Mental defect. Restlessness, a very fleeting attention and screaming attacks along with retardation of the usual signs of normal mental development indicated definite mental deficiency.

Case. No. 30.

v. Pfaundler. (1913).

Infant, 1 month. Facial paralysis. Severe degree of diplegia. Details of distribution not available.

Ocular paralysis. Bilateral abducens palsy. Strabismus not mentioned.

Lingual paralysis. Right-sided.

Club foot, on the left side.

Case No. 31.

Beetz. (1913).

Female. 22 years. A sister of Case nos. 32 and 33. A fourth sibling, a girl who died aged fifteen months, was said to have had a mask-like face and to have been unable to close her eyes from birth. This was almost certainly a case of congenital facial diplegia also. This family lived in an isolated valley of the Black Forest where consanguinity is notorious, there were two inter-marriages in the three previous generations.

Facial paralysis. There was slight facial asymmetry. There was complete frontalis palsy on both sides and paresis of the other facial muscles, most marked in the orbiculares oculi and oris muscles.

Palatal paresis. Slight bilateral weakness of the soft palate was present.

Pectoralis muscle defect. Right-sided with corresponding mammary hypoplasia.

Ear deformity, slight.

Congenital dislocation of the right hip.

Case No. 32.

Beetz. (1913).

Male. 20 years. Brother of Case Nos. 31 and 33.

Facial paralysis. Facial asymmetry of severe degree. Palsy most marked in the frontalis orbicularis oculi and orbicularis oris muscles.

Ocular paralysis. Unilateral abducens paresis, slight, right-sided. Bilateral ptosis, partial.

Trigeminal paresis. Weakness of the chewing muscles.

Muscle defects, multiple. Several scapular muscles on both sides showed defective development. Bilateral serratus anterior defect, complete on the right and partial on the left. In addition, all three parts of the trapezius, particularly the upper, the levator scapulae, the supra- and infra-spinati and the latissimus dorsi showed partial defect on the right side, while the latter two were similarly affected on the left.

Ear deformity, slight. Arched palate.

Mental defect, of moderate degree.

Hypermetropia and astigmatism were present.

Case No. 33.

Beetz. (1913).

Female. 7 years. A sister of Case Nos. 31 and 32.

Facial paralysis. There was facial asymmetry. There was complete bilateral frontalis palsy and paresis of the other facial muscles.

Ocular paralysis. Unilateral abducens palsy, complete, left-sided. No strabismus.

Palatal paresis. A slight degree of paresis of the soft palate on both sides was noticed.

Ear deformity, slight, bilateral.

Case No. 34.

Snowball. (1915).

Female. 1 years. There was nursing difficulty in infancy, inability to close the eyelids completely was also noticed.

Facial paralysis. Slight facial asymmetry, the right cheek being fuller and rounder than the left. Palsy almost complete, the only moveable muscles being those at the right corner of the mouth.

Ocular paralysis. Bilateral abducens palsy, complete. Convergent strabismus in both eyes.

Case No. 35.

Kahlmeter. (1916).

Male. 38 years. Derangements of eyes and face noticed at birth. Could not close the eyelids or move the eyes. Mental development was considerably retarded. Walked at five years and talked still later, not clearly until eight years. Did badly at school owing to subnormal mentality. Also displayed nervous instability. The patient's voice never broke. Spent several of later years in hospital with keratitis and chronic ulcers of the feet. Some toes were amputated. Also had frequent chronic sores on the forehead for some years. He was thought to be luetic.

Facial paralysis. Complete immobility of the upper part. Fair movement around the mouth but unable to whistle. The skin and subcutaneous tissues were atrophic particularly in the upper part of the face. Electrical reactions negative in the upper face and diminished in the lower.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial. Atypically the lateral recti functioned well, also the superior. Complete palsy of /

of the medial and inferior recti. State of the obliques uncertain. Bilateral divergent strabismus of severe degree. Immobility of right pupil, left reacted normally. No synechiae in either. Both circular and dilated with mydriatics.

Myopia of severe degree also keratitis and corneal opacities.

Mental defect, of moderate degree. Unstable temperament.

Infantilism, unbroken voice, absence of hair growth on the face and in the axillae and scanty on the pubis. Infantile genitalia.

High sugar tolerance.

No evidence of lues was ever obtained.

Case No. 36.

Gütermann. (1917).

Male. 7 months. After birth inability to suck was noticed. Could suck the teat of the bottle if the hole was large enough and it was placed deeply in the mouth.

Facial paralysis. Skin of the face thin and stretched. Face slightly thinner on the right. Immobile and free from wrinkles. Mouth always slightly open with dribbling. Only facial movements were those of the left mouth corner and the underlip on both sides. Electrical responses were only obtained in these muscles.

Ocular paralysis. Bilateral abducens palsy. Convergent strabismus in both eyes.

Lingual paralysis. Tongue slightly curled on the floor of the mouth. On protrusion tip deviated towards the right. Right half thinner than the left.

Pectoralis muscle defect. The sterno-costal part of the pectoralis major and the pectoralis minor were absent. The skin in that region was thin and stretched.

Brachial deformity. Hypoplasia of the muscles. Highly /

Highly placed right scapula which caused an apparent shortening of the arm. Syndactyly of the second to fifth fingers on the same side.

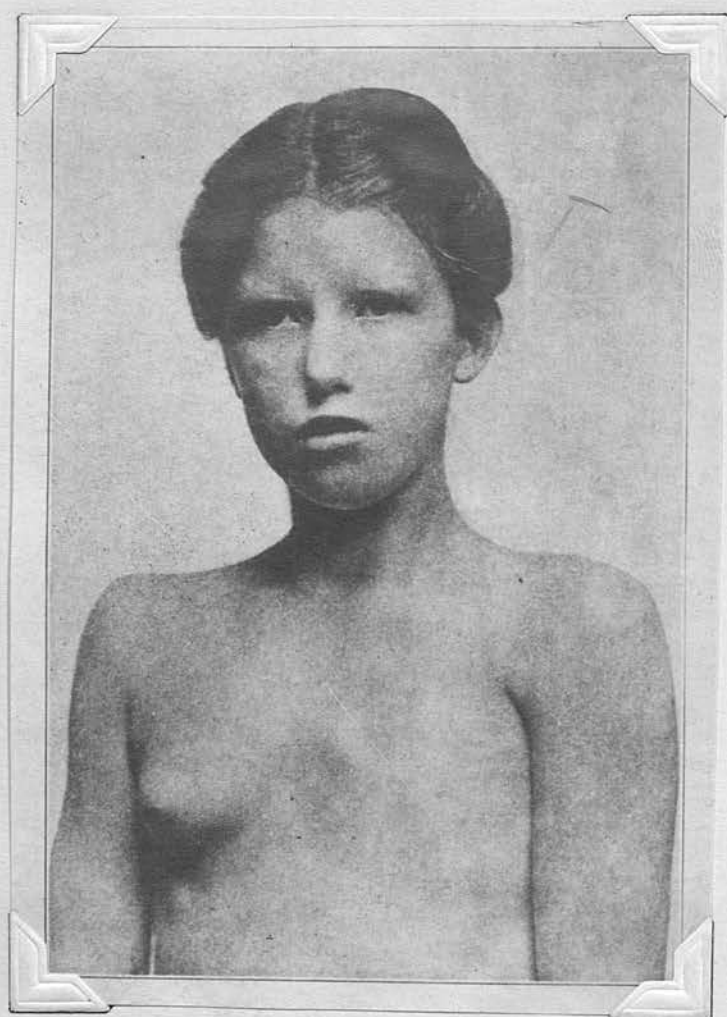
Lachrymal caruncles, aplastic on the left and hypoplastic on the right.

Case No. 37.

Fry. (1918).

Infant. 1 month. Nursing difficulty noticed the day after birth.

Facial paralysis. Incomplete closure of the eyelids when asleep. Mouth partially opened and lower lip everted. Complete paralysis of the lower right side of the face apart from the platysma. Paresis of the upper right side and the entire left side.



Case No. 38.

Fry & Kasak. (1919).

Female. 1 year.. Father and two brothers of mother had congenital defects. Was a tradition of syndactyly of the second and third toes in the mother's family. Parents were always aware of the anomalies.

Facial paralysis. Incomplete closure of the eyelids. Dribbling of saliva. Only facial movements were slight drawing down of the mouth corners by the platysmae, rather more on the left.

Ocular paralysis. Bilateral abducens palsy. No strabismus.

Trigeminal paresis. No lateral movements of the mandible.

Brachial deformity. Left arm rather smaller than the right, the hand markedly so. The second and fifth fingers were particularly small.

Mammary aplasia on the left.

Case No. 39.

Abrahamson. (1921).

Female. 4 years. Nursing difficulties.

Facial palsy noticed at three months. Fits in infancy.

Facial paralysis. No wrinkling of the forehead. Paresis on both sides of the face. Left mid-facial region more active than the right. On attempting to screw up the eyes face drawn up on right and flattened on left.

Ocular paralysis. Bilateral abducens paresis, worse on the left, with limited lateral movements of the eyes. No strabismus.

Lingual paralysis. Tongue thinner on the left and deviates to the left on protrusion.

Case No. 40.

Cadwalader. (1922).

Female. 13 years. Parents first cousins.

Brother is affected by exactly the same condition which was noticed at birth. Nursing was difficult. Could not move the lips or facial muscles. Parents became alarmed at four months as the child had not smiled.

Facial paralysis. Complete diplegia.

Deafness, severe on both sides.

Case No. 41.

Cadwalader. (1922).

Female. 10 years. Had difficulty in sucking the bottle. Anomalies first noticed at one month, when observed strabismus and inability to close the eyelids, also facial palsy, particularly on the right.

Facial paralysis. Only movements were drawing down of the mouth corners by the platysmae.

Ocular paralysis. Bilateral abducens palsy. Both eyes can be rotated up and down but not symmetrically. On elevation the lower border of the right cornea is at a lower level than that of the left. Pupils do not react to convergence. No strabismus.

Case. No. 42.

Kirby. (1923).

Male. 52 years. Contracted lues at forty and came under observation with tabes dorsalis. The congenital anomalies were noticed in early infancy.

Facial paralysis. Ectropion present. Almost complete diplegia. Electrical responses obtained from both the zygomatici and both quadratus lab. sup. on both sides.

Ocular paralysis. Bilateral abducens palsy. Power of convergence diminished. No strabismus.

Lingual paralysis, bilateral. Deviated to the left on protrusion. Thin and wrinkled.

Club foot, unilateral. Right talipes equinovarus.

Case. No. 43.

Cameron. (1924).

Male. 31 years. Facial paralysis. Complete
diplegia.

Ocular paralysis. Bilateral ophthalmoplegia
externa. Eye movements very restricted, particularly
the lateral.

Club foot. Bilateral talipes equino-varus.

Brachial deformity. Fingers of the right
hand webbed and deformed.

Case No. 44.

Van Gelder & Weyl. (1927).

Male. 53 years. A sister was epileptic. Drinking difficult from the first. Eating also difficult. Speech always abnormal. Was always clumsy and backward.

Facial paralysis. Uses hand on outside of cheek to push food back into the mouth and pours fluid into the mouth with the tongue under the glass. Face expressionless. Complete diplegia.

Ocular paralysis. Bilateral ophthalmoplegia externa. Only movement is a slight downward rotation. No strabismus. Bilateral ptosis, partial.

Lingual paralysis. Marked palsy and atrophy of the right half of the tongue. On protrusion deviated to the right.

Trigeminal paresis. Could not make a chewing motion.

Palatal paresis. Soft palate moved sluggishly. There was dysphagia.

Brachial deformity. Hands are not symmetrical. Both /

Both are deformed, more so on the radial side. The first, second and third fingers are short and thick. Syndactyly between the second and third fingers, worse on the right side.

Ear deformity. Slight on both sides.

Arched palate.

Conjunctivitis and corneal opacities.

Was regarded as "simple" but the impression of mental defect was apparent rather than real.

Case No. 45.

Mandels. (1928).

Male. 15 years. Anomalies present since childhood.

Facial paralysis. There was a severe degree of diplegia, no details were given.

Ocular paralysis. Bilateral ophthalmoplegia externa. Only slight vertical movements were possible. Bilateral convergent strabismus of severe degree. At operation the external recti muscles were found to be very hypoplastic.

Dysphagia was present.

Pectoralis muscle defect. Absence of part of the left pectoralis major and of the minor and hypoplasia of the other muscles on the same side of the chest. Cartilage defects of the third, fourth and fifth ribs on the same side.

Brachial deformity. Hypoplasia of the left arm muscles.

Conjunctivitis, myopia and astigmatism.

Mental defect. Not severe but intelligence subnormal.

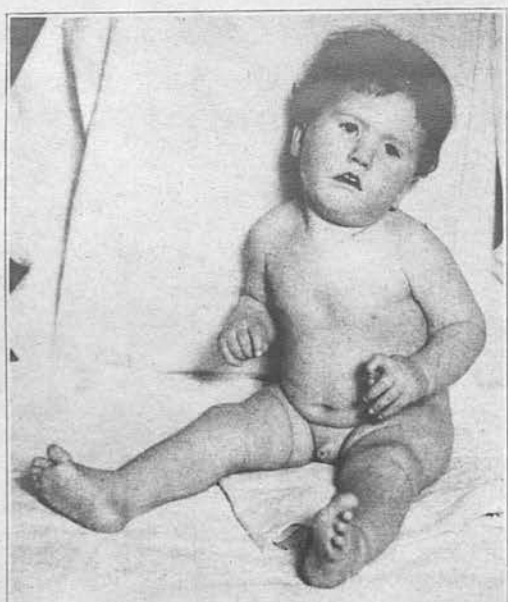


Fig. 2.—Appearance of child during repose.



Fig. 1.—Appearance of child while crying.

Case No. 46.

Bonar & Owens. (1929).

Male. 9 months. Nursing was rather difficult.

Expressionless face noticed a few days after birth. The mouth was always partly open and epiphora was noticeable. Recurrent conjunctivitis occurred. Until nine months mother thought sub-normal mentally but not after that.

Facial paralysis. Complete diplegia.

Electrical reactions negative, but over thirty milliamps. contractions of all facial muscles occurred with galvanism.

Ocular paralysis. Bilateral ptosis, slight.

Club foot, unilateral. Talipes equino-varus on the left.

Epicanthic folds, an arched palate and an unusually broad root of the nose were other features.

Case No. 47.

Alajouanine, Huc & Gopcevitch. (1930).

Female. 6 years. Immobile face, squint and club foot noticed at birth. As grew older mother was more struck by the immobile face and the difficulty in knowing whether the child was laughing or crying. Unable to suck in infancy. No dysphagia.

Facial paralysis. Upper lip prominent, lower slightly inverted, eyelids incompletely closed during sleep. The only voluntary movement of the face was a drawing outwards of the left mouth corner.

Ocular paralysis. Bilateral abducens palsy. Bilateral convergent strabismus.

Club foot, bilateral talipes equino-varus.

Brachial deformity, unilateral. Club hand on the right side.

Case No. 48.

Alajouanine, Huc & Gopcevitch. (1930).

Female. 5 years. Condition of the eyes and feet noticed at birth. Difficulty with nursing. Mother thought blind owing to constant convergence and upward deviation of the eyes. Convergent strabismus of the eyes, permanent during the whole of the first year. Afterwards became progressively less constant and then transitory.

Facial paralysis. Prominent upper lip, lower slightly inverted. No movement on laughing or crying. A slight outward and downward drawing of the right mouth corner was the only voluntary movement. Slight electric responses were obtained in the buccinators, the orbicularès palpebrarum and orbicularis oris muscles.

Ocular paralysis. Bilateral abducens palsy, complete. Bilateral strabismus, convergent and slight, rather worse on the left.

Lingual paralysis. The right half of tongue thinner than the left, both edges wrinkled. On protrusion tip deviated to the right.

Club foot. Bilateral talipes equino-varus.

Case No. 49.

Alajouanine, Huc & Gopcevitch. (1930).

Male. 1 year, 9 months. Squint and club foot noted at birth. Convergent strabismus which was permanent at first later became transitory. The eyelids were incompletely closed during sleep. Could not nurse. Had dysphagia and nasal regurgitation. Mother was struck by the facial immobility and did not know whether the child was laughing or crying. Had not begun to speak.

Facial paralysis. Prominent upper lip, lower slightly inverted. Complete diplegia.

Ocular paralysis. Bilateral abducens palsy, complete. Bilateral convergent strabismus.

Club foot. Bilateral talipes equino-varus.

Mental backwardness probably due to physical condition.

Case No. 50.

Alajouanine, Huc & Gopcevitch. (1930).

Female. 4 months. Expressionless face, fixity of vision and club foot were noticed at birth. No nursing difficulty. Mother thought the child blind. The convergent strabismus, permanent for the first few weeks, then became intermittent. Mother's attention was attracted by the expressionless face on laughing and crying, the child "laughs in her throat."

Facial paralysis. Prominent upper lip, lower sometimes inverted. Absence of winking a striking feature. Complete diplegia.

Ocular paralysis. Bilateral abducens palsy, complete. Bilateral convergent strabismus, slight.

Club foot. Bilateral talipes equino-varus.



Abb. 1.

Case No. 51.

Ullrich. (1930).

Female. 8 years. At birth a greatly swollen condition of the neck was noticed, also swellings on the right hand and both feet. The foot swellings gave the impression of deformities, the skin on the hand and particularly on the feet was a bluish-red colour. During the whole of the first year finger impressions remained for a long time on the thick coarse polsters of the hand and feet. The swellings disappeared during the second year. Owing to the expressionless face mental defect was feared.

Facial paralysis. The down-hanging angles of the mouth gave it a triangular form. The facial musculature was paretic on both sides, though no movements were absent all were sluggish and the face was always somewhat mask-like.

Ocular paralysis. Ptosis, bilateral and of severe degree.

Pterygium colli. The most conspicuous malformation was a broad skin-fold on either side of the neck stretching from the ear to the acromion process. /

process.

Ears. Deep set with ingrown lobes.

Arched palate.

Mammae, hypoplastic.

Hair border reaches far down nape of neck.

Case No. 52.

Yealland. (1931).

Female. 16 years. A sister was epileptic.

Unable to nurse or close eyelids from birth.

Facial paralysis. Diplegia almost complete.

Eyes can be partially closed with effort and some fibres of the platysma contract on trying to show the teeth. Electrical reactions negative.

Ocular paralysis. Ophthalmoplegia externa, bilateral and partial. Only up and down movements are possible. Pupils do not react to accommodation.

Lingual paralysis, bilateral. Tongue abnormally small, deformed and wrinkled, especially on the left.



Abb. 1.

Case No. 53.

Spatz & Ullrich. (1931).

Male. 3 months. Immobility of the face and constantly open eyes and mouth were noticed at birth. Breast feeding was not attempted. Conjunctivitis appeared at four weeks. The infant became increasingly marasmic and died of broncho-pneumonia aged three months.

Facial paralysis. The depressed mouth corners gave it a triangular appearance. On crying the left mouth corner was drawn down. This was the only facial movement.

Ocular paralysis. Bilateral ophthalmoplegia externa, total. The only eye movement was a fine rotary nystagmus. Pupils, light reflex absent but atropine made them irregular and iris prolapse soon followed.

Brachial deformity. There was webbing between single fingers.

Ears, deep set.

Root of nose broad and flat.

Hyperthelia, right-sided.

Pathology, see text.

Case No. 54.

Allen. (1931).

Male. 10 years. Facial paralysis. Complete diplegia.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial. In addition to complete abducens palsy there was limitation of upward and inward movement. On looking down the eyes turned inwards.

Brachial deformity. Bilateral syndactyly of index and middle fingers.

Club foot. Bilateral talipes equino-varus.

Congenital alexia.

Slight hydrocephalus.

Epilepsy.

Case No. 55.

Bielschowsky. (1932).

Female. 9 years. Anomalies present from birth.

Facial paralysis. Complete diplegia.

Ocular paralysis. Bilateral abducens palsy,
complete. No strabismus or diplopia.

Myopic astigmatism.

Case No. 56.

Garrahan & Cucullú. (1932).

Male. 2 years, 3 months. Peculiarities of face and feet noticed at birth. At two months it was noticed that the usual gestures were absent on crying. No nursing difficulty.

Facial paralysis. Expressionless face, mouth always open, a prominent upper lip, nasal speech and mispronunciation of certain words were all present. Complete diplegia. Electrical reactions negative.

Ocular paralysis. Bilateral abducens palsy. Convergent strabismus, bilateral.

Club foot. Bilateral talipes equino-varus.

Arched palate.

Lachrymal ducts, slightly stenosed.

Hypermetropia.

Case No. 57.

Garrahan & Cucullú. (1932).

Female. 2 weeks. Deformities of limbs noticed at birth. At two weeks the mother took to clinic because of nursing difficulty and expressionless face.

Facial paralysis. Complete diplegia.
Electrical reactions negative.

Ocular paralysis. Bilateral abducens palsy.
Convergent strabismus, bilateral.

Lingual paralysis, bilateral. The tongue was arched in each half and could not be protruded satisfactorily. There was great difficulty in sucking, with a flow of fluid from the nostrils.

Brachial deformity, aplasia and flexion deformity of the fingers of the left hand.

Club foot. Bilateral talipes equino-varus.
Bifid uvula.

Epicanthus.

Wassermann reaction, negative.

Arsenical treatment was begun at nine months and continued for several months.

Case No. 58.

Babonneix & Miget. (1932).

Female. 5 years. Facial asymmetry, suckling difficulty and dysphagia were noticed soon after birth. Lingual palsy was first noticed at about three years on account of delayed speech.

Facial paralysis. Expressionless face striking, mouth half open. The upper lip was prominent and the lower inverted. Slight asymmetry at rest indicating left facial palsy, voluntary movement exaggerated the asymmetry causing the left palsy to be more prominent and revealing a slight palsy on the right side also. Electrical reactions, negative on the left and diminished on the right.

Ocular paralysis. Bilateral ophthalmoplegia externa, partial. Abducens palsy on both sides, worse on the left. Convergent strabismus also bilateral and worse on the left side. Other details of ocular palsies not given.

Lingual paralysis, bilateral. Tongue small and thin. Protrusion poor and without deviation, little movement owing to severe involvement. Fibrillary twitchings were present. Speech nasal and monotonous.

Nose broad at the base.

Case No. 59.

Gareiso & Barbieri. (1933).

Female. 5 years. The expressionless face, the club foot and squint were noticed at birth. First walked at three years and was equally slow in speaking.

Facial paralysis. The mouth was open, the upper lip prominent and the lower rather inverted. Complete diplegia. Electrical reactions, the frontalis and the orbicularis oris muscles responded to F. and G.

Ocular paralysis. Bilateral abducens palsy. Convergent strabismus, bilateral. Bilateral ptosis, partial.

Mental defect. Attention very fleeting, replied "yes, yes" to everything.

Nose rather flattened.

Bordet - W.R. weak + .

Case No. 60.

Decourt & Perreau. (1935).

Male. 9 years. The club foot, incomplete closing of the eyelids and squint were noticed at birth. A little later the parents were struck by the absence of expression.

Facial paralysis. The mouth was always open and labial sounds could not be made. Absence of expression more striking on talking, etc. The face looked thin and "atrophic", the eyelids could not be closed completely. The only facial movements were an outward and downward drawing of the mouth corners and a contraction of the platysma, especially on the right side. Electrical reactions, weak responses to F. and G. in lower facial regions.

Ocular paralysis. Bilateral abducens palsy. Convergent strabismus, bilateral and severe.

Club foot, Bilateral talipes equino-varus.